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State of the Science Review

New and emerging infectious diseases (Ebola, Middle Eastern respiratory syndrome coronavirus, carbapenem-resistant *Enterobacteriaceae*, *Candida auris*): Focus on environmental survival and germicide susceptibility

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In the recent past, we have witnessed the emergence of many new infectious diseases, some of which are major public health threats. The public health threats posed by emerging diseases have been well described in 2 reports from the Institute of Medicine, 1 in 1992 and 1 in 2001.[1,2] Since the outbreak of *Legionella* in 1976[3,4] and AIDS in 1981[5,6] later demonstrated to be due to HIV in 1983,[7] many emerging infectious diseases have had important infection control implications. This review will focus on several of the most important current infection prevention threats including Ebola virus, Middle Eastern respiratory syndrome (MERS) coronavirus (CoV), carbapenem-resistant *Enterobacteriaceae* (CRE), and *Candida auris* with a focus on mechanisms of transmission, environmental contamination and stability, and germicide susceptibility. Germicides that will be discussed include chemical sterilants used to process critical equipment and devices (eg, surgical instruments, implants), high-level disinfectants that are used to disinfect semicritical equipment and devices (ie, medical equipment or devices that come into contact with nonintact skin or mucous membranes), low-level disinfectants used for disinfection of surfaces or shared equipment that come into contact with intact skin (eg, blood pressure cuffs, room surfaces), and antiseptics (ie, germicides used on skin or mucous membranes to reduce the microbial flora).[8,9] This review updates a previous article that reviewed Ebola and MERS and also reviews CRE and *C auris*.[10]

DEFINITIONS

The World Health Organization (WHO) states, "an emerging disease is one that has appeared in a population for the first time, or that may have existed previously but is rapidly increasing in incidence or geographic range."[11] The Centers for Disease Control and Prevention (CDC) provides the following definition of emerging infections as "infectious diseases whose incidence in humans has increased in the past 2 decades or threatens to increase in the near future have been defined as 'emerging.'" These diseases, which respect no national boundaries, include: (1) new infections resulting from changes or evolution of existing organisms; (2) known infections spreading to new geographic areas or populations; (3) previously unrecognized infections appearing in areas undergoing ecologic transformation, and (4) old infections reemerging as a result of antimicrobial resistance in known agents or breakdowns in public health measures.[12]

FACTORS IN THE EMERGENCE OF INFECTIOUS DISEASES AND PREPAREDNESS

The factors leading to the emergence of infectious diseases have been described.[13-17] Importantly, all these authors noted that we will continue to see new and emerging infectious diseases for the foreseeable future. Recent articles have provided recommendations for preparedness at the health care facility, local and national levels.[10,18-20]

KEY CONSIDERATIONS IN ASSESSING AND MANAGING THE THREAT OF EMERGING INFECTIOUS DISEASES IN HEALTH CARE FACILITIES

Assessing and managing the threat of an emerging infectious disease requires an understanding of the biology of the pathogen, its epidemiology, the clinical manifestations of infection, the methods of

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diagnosis, and therapies (if available).[10] All health care facilities should have a highly communicable disease plan for agents that are transmitted by droplet or aerosols (eg, severe acute respiratory syndrome [SARS], MERS) or are transmitted by contact (eg, Ebola, Lassa).[10] Detailed information is best found, especially early in an epidemic, on the web pages of local and state health department, the CDC, and the WHO. For highly communicable diseases, there are 2 major areas that place a health care facility and the personnel at substantial risk for disease acquisition and transmission.[10] First, inadequate screening procedures when patients enter a health care facility can potentially allow transmission from an ill patient to health care personnel, other patients, or visitors. Second, inadequate supplies of personal protective equipment (PPE) and/or training of health care personnel (HCP) in proper donning and doffing procedures can increase the risk of exposure for HCP.

A key focus of this article is to review the transmission routes of new and emerging infectious agents. Preventing disease acquisition via person-to-person transmission or contact with the contaminated environment depends on rapid and appropriate institution of isolation precautions, appropriate hand hygiene, and appropriate disinfection of medical equipment, devices, and the surface environment. Importantly, once the nature of the emerging disease is known (ie, enveloped virus, bacteria, fungi, nonenveloped virus, mycobacteria), it is possible to determine the proper antiseptics and disinfectants, even in the absence of studies of the exact infectious agent.[21] For example, an enveloped virus (eg, Ebola, MERS-CoV) or vegetative bacterium (eg, CRE) would be inactivated by any agent active against nonenveloped viruses or mycobacteria. It is important to remember that alcohol has reduced activity against nonenveloped viruses (eg, norovirus) and no activity against spores (eg, *Clostridioides difficile*).

EBOLA

History and microbiology

The first recognized outbreak of Ebola occurred in West Africa in 1976. In the 40 years since the initial outbreaks in Zaire and Sudan, >20 outbreaks have occurred.[22] The largest outbreak occurred in West Africa (Guinea, Sierra Leone, and Liberia) from 2014-2016, and resulted in 28,600 cases and 11,325 deaths.[23] Importantly, in the 2014-2016 outbreak >850 HCP developed confirmed or probable Ebola virus disease (EVD).[24] The percentage of exposed HCP who developed EVD has ranged from 12.5%-76%.[24] The mortality of HCP who developed Ebola has frequently exceeded 50%.[24] Key concerns for HCP include the low inoculating dose required for transmission; high frequency of HCP infections, especially in resource poor countries; and high mortality. As of 2019, an EVD outbreak is continuing with moderate intensity in the Democratic Republic of the Congo.

Overall, 11 people were treated for Ebola in the United States during the 2014-2016 epidemic.[23] Two out of 149 HCP who cared for a patient with EVD in the United States developed EVD; both recovered.[24]

The microbiology, epidemiology, diagnosis, clinical features, and treatment of Ebola have been reviewed.[22,25-30] Ebola is caused by a nonsegmented, single-stranded negative RNA virus of the family Filoviridae. There are 5 identified Ebola virus species, 4 of which are known to cause disease in humans: Zaire, Sudan, Tai Forest (formerly Cote d'Ivoire), and Bundibugyo. The fifth, Reston virus, has caused disease in nonhuman primates, but not in humans. The natural reservoir host of Ebola virus remains unknown. However, the detection of antibodies against Ebola and Ebola virus fragments in fruit- and insectivore bats are highly suggestive that these animals serve as a reservoir.

EVD is characterized by the sudden onset of fever, headache, myalgias, arthralgias of the large joints, and back pain. Typically, 2-3 days after the initial symptoms gastrointestinal symptoms occur including abdominal pain, nausea, vomiting, and diarrhea. A macular or maculopapular skin rash may appear on days 5-7 of the disease. Hemorrhage is less common, occurring in only 15%-20% of patients. Terminal cases develop disseminated intravascular coagulation, septic shock, and multiorgan system failure. Mortality ranges from 40%-90% and depends, in part, on the infecting strain.

Epidemiology and transmission

Ebola is transmitted person-to-person most commonly through direct contact (ie, nonintact skin or via mucous membrane contact) with blood, body fluids (eg, urine, saliva, sweat, feces, vomit, breast milk, and semen) of an ill person, or indirectly via objects such as needles and syringes that have been contaminated with body fluids from an ill person (Table 1).[31] Less common mechanisms include acquisition from infected fruit bats or nonhuman primates. Sexual transmission has also been described. Ebola is not transmitted via the air or by water. However, in Africa it has been acquired by handling bush meat. The incubation period of Ebola is generally 8-10 days (range, 2-21 days). Person-to-person transmission has only occurred from persons with signs or symptoms of EVD. Diagnostic testing is achieved with the use of real time (RT) polymerase chain reaction (PCR) on blood.[32] Viral RNA is usually detectable by PCR between 3 and 10 days after the onset of symptoms.

Patients with EVD should be provided appropriate critical care including fluid and electrolyte replacement; oxygen therapy to maintain oxygen status; medications to support blood pressure, reducing vomiting and diarrhea, and to manage fever and pain; oral or parenteral nutrition; and treating coexisting infections (eg, malaria), if present.[33-34] Although there are currently no antiviral drugs approved by the US Food and Drug Administration (FDA), a number of therapies are under investigation including antibody-based therapies (eg, convalescent blood products, monoclonal antibodies), and drugs and small molecules (eg, Ebola virus gene expression inhibitors, and Ebola virus entry and inhibitors).[33-35] A number of preventive vaccines are currently in clinical trials.[33-35]

Environmental contamination and survival

Ebola virus has been isolated by cell culture from multiple body fluids of infected or convalescent patients including blood, saliva, stool, vaginal fluid, sweat, and urine for days or months after illness.[36] Given the high volume of diarrhea and vomiting and the potential for fomite transmission, the frequency of environmental contamination and survival of Ebola virus is of high concern. Several studies have assessed the frequency of contamination within the health care

Table 1
Modes of transmission of Ebola virus

Common
• Person-to-person via direct contact via body fluids (ie, urine, saliva, sweat, feces, vomit, breast milk, and semen)
• Person-to-person via indirect contact due to environmental contamination (eg, needles, syringes)
Less Common
• Infected fruits bats
• Nonhuman primates (eg, apes, monkeys)
• Sexual transmission via semen from a man who recovered from Ebola virus disease (via oral, vaginal, or anal sex)
• Ingestion of bush meat
• Exposure in a laboratory

environment of a patient with EVD by culture[37,39] or RT-PCR.[37-42] Although the frequency of environmental contamination was variable, all studies reported some environmental samples were positive by RT-PCR. Contamination was most often demonstrated for blood stained items,[37,42] and toilet/latrine,[39,40,42] or objects in close proximity to the patient (eg, mattress, bed rails).[37,42] Samples from PPE (eg, gloves) have tested positive by RT-PCR for Ebola virus.[37,42] Viable virus was not isolated in either of the 2 studies that cultured environmental samples.

The environmental survival of Ebola virus has been studied using culture-based techniques under a variety of environmental conditions (eg, temperature, humidity), in various liquids, aerosols, and surfaces.[43-49] These studies may be summarized as follows. First, viable Ebola can survive in liquids (eg, liquid media, tissue culture media, water, liquid blood, plasma) for days to weeks. Second, viable Ebola virus can also survive dried on a variety of surfaces (eg, plastic, glass, stainless steel, polypropylene, nitrile, bank notes) for days to weeks. Third, Ebola survives in liquids and on surfaces for a longer duration of time at lower temperatures (eg, 4°C vs 21°C). Fourth, although aerosol transmission has not been observed, Ebola virus has been demonstrated to survive in an aerosol for >3 hours. Fifth, survival of Ebola on porous surfaces, such as cotton, is substantially less than on steel and plastic surfaces.

Using macaques, viable Ebola virus was demonstrated to survive in corpses for at least 3 days and RNA could be detected for tissues for the entire 10-week study period.[50] Ebola virus was detected by RT-PCR in a deceased patient's house 14 days after a patient was buried.[41] Consistent use of appropriate PPE with strict adherence to donning and doffing protocols is crucial to preventing acquisition of EVD during patient care.[28,51,52] A key component of reducing HCP risk is proper training in PPE donning and doffing with ongoing training to maintain competency.

Susceptibility to germicides

Ebola virus is not inactivated by detergents.[53] Using RT-PCR, Cook et al[54] demonstrated that Ebola virus outbreak variants dried with an organic soil load on a stainless steel carrier were inert after 5 minutes exposure to sodium hypochlorite (≥0.5%) and after 2.5 minutes exposure to 70% ethanol. Smither et al[55] confirmed the activity of sodium hypochlorite; 10^4 Ebola viruses as measured by PCR were inactivated by 0.75% sodium hypochlorite with 10 minutes contact time. In a later study, Smither et al[56] reported that multiple disinfectants (ie, 0.5% hypochlorite, 10% hypochlorite, 5% peracetic acid, 70% ethanol) were effective against dried cell culture medium containing Ebola virus. However, only 5% peracetic acid consistently reduced Ebola virus titers in dried blood to undetectable levels. Based on the hierarchy of microbial susceptibility to germicides and studies of germicide efficacy, the CDC states that any US Environmental Protection Agency-(EPA) registered hospital disinfectant with a label claim for a nonenveloped virus (eg, norovirus, rotavirus, adenovirus) can be used to disinfect environmental surfaces in rooms of patients with known or suspected EVD.[57]

In a systematic review, Kampf[58] reported that 80% ethanol was highly effective against all 21 tested, enveloped viruses within 30 seconds. A >4-$\log_{10}$ reduction of an Ebola strain was achieved in 15 seconds using the following povidone-iodine solutions: 4%, 7.5%, 10%, and 3.2% iodine with 78% alcohol.[59] Therefore, data suggests that hand antisepsis for skin contamination with Ebola virus can be obtained with either povidone-iodine or 70%-80% alcohol (although proper PPE should always be worn).

An ultraviolet-light (UV-C) booth was demonstrated to inactivate >3-$\log_{10}$ bacteriophage MS2 (a nonenveloped virus) and could be useful for disinfection of contaminated PPE.[60]

MERS

History and microbiology

The history of MERS has been reviewed.[61-63] MERS, a new viral respiratory disease of humans, was first described in 2012 and later discovered to be caused by a novel coronavirus, MERS-CoV (lineage 2C β CoV). The WHO has reported that between 2012 and December 2018, there were 2,279 laboratory-confirmed cases of MERS, including 806 associated deaths (case-fatality rate = 35.3%), reported globally.[64] Although cases have been reported from 27 countries, the majority of cases (ie, 1,901) have been reported from Saudi Arabia.[64] Two cases of MERS have been reported in the United States, both of whom were health care providers who acquired infection in Saudi Arabia.[65] No transmission has been reported in the United States.

The microbiology, epidemiology, and clinical manifestations of MERS have been reviewed.[66-72] MERS-CoV, a betacoronavirus, is a single-stranded, positive-sense enveloped RNA virus that can cause an acute respiratory illness in humans. MERS-CoV is a zoonotic disease that is transmitted from animals-to-humans. Dromedary camels, hosts for MERS-CoV, have been implicated in direct and indirect transmission to humans, although the exact mode of transmission is unknown.[63,67,71] Bats are likely the main mammalian reservoir.[71]

The clinical spectrum of MERS infection ranges from asymptomatic or mild respiratory symptoms to severe acute respiratory disease and death. Typical symptoms of MERS include fever, cough, and shortness of breath. Pneumonia is common but not always present. Gastrointestinal symptoms (vomiting, diarrhea) frequently occur. Risk factors for more severe disease include older age, comorbidities (eg, chronic lung diseases, diabetes), and immunosuppression. The diagnosis is confirmed by a positive RT-PCR assay targeting at least 2 different genomic regions. Currently, there are no specific therapies or vaccines available.

Epidemiology and transmission

MERS may be transmitted from person-to-person via direct contact likely due to droplet transmission (Table 2). This occurs most commonly when there is close contact such as providing unprotected care to an infected patient. Thus far, no sustained community transmission has been documented. Studies of family clusters and HCP contacts of patients have reported low frequencies of transmission (ie, 1%-3%). However, increased transmission has occurred in health care settings with limited infection control procedures. Importantly, MERS may be transmitted from an asymptomatic source.[73] However, super spreaders have also been reported.[74]

The epidemiology and prevention of MERS in health care settings has been reviewed.[10,75-77] Infection prevention strategies have been informed by the multiple reports of outbreaks of MERS involving health care facilities,[78-81] and by the large outbreak in South Korea.[82] Importantly, during these outbreaks >20% of cases may have occurred in health care providers. Factors contributing to intrahospital transmission include: (1) the initial symptoms of MERS are nonspecific

Table 2
Modes of transmission of Middle Eastern respiratory syndrome coronavirus

Transmission Well Established
• Human-to-human transmission via direct contact due to droplet spread (source may be asymptomatic)
• Animal-to-human transmission (dromedary camels to humans)
Transmission Unclear
• Human-to-human transmission via direct contact due to airborne transmission
• Human-to-human transmission via indirect contact (ie, fomites, contaminated surfaces)

leading to a failure to isolate the patient; (2) inadequate compliance with infection control practices; (3) inadequate health care facilities (eg, overcrowding, close proximity of patients to cases); (4) use of aerosol generating procedures; and (5) prolonged viral shedding.[83]

Environmental contamination and survival

Extensive environmental contamination has been documented by both culture and RT-PCR in clinical areas housing MERS patients.[84,85] Positive sites have included patient room surfaces (eg, bed sheets, bedrails, intravenous fluid hangers), anteroom surfaces, medical devices (eg, portable x-ray machines, thermometers), and air-ventilating equipment. Touchable surfaces have been found to be contaminated through respiratory secretions from clinically fully recovered patients.[84] MERS-CoV has also been detected in air samples in the vicinity of patients.[85] However, 1 large outbreak evaluation failed to demonstrate any transmission via the potentially contaminated environment without direct contact with the index case.[86]

MERS-CoV has been shown to be recoverable after 48 hours on steel or plastic washers (20°C and 40% relative humidity).[87] Further, no decrease in stability was observed during aerosolization experiments. Multiple studies on CoVs other than MERS-CoV have demonstrated that these viruses can remain viable for days to weeks on environmental surfaces.[88,89] Survival is enhanced at low temperatures (ie, 4°C vs 20°C).[89]

Susceptibility to germicides

As MERS-CoV is an enveloped virus, it is likely susceptible to EPA-registered hospital disinfectants and FDA-approved antiseptics. Studies on inactivation of surrogates for SARS-CoV (mouse hepatitis virus and transmissible gastroenteritis virus) demonstrated the following inactivation after 1-minute contact time: (1) for transmissible gastroenteritis virus, there was a $\log_{10}$ reduction factor of 3.2 for 70% ethanol, 2.0 for phenolic, 2.3 for ortho-phthalaldehyde, 0.35 for 1:100 hypochlorite, 4.0 for 62% ethanol, and 3.5 for 71% ethanol; and (2) for mouse hepatitis virus, $\log_{10}$ reduction factors were 3.9 for 70% ethanol, 1.3 for phenolic, 1.7 for ortho-phthalaldehyde, 0.62 for 1:100 hypochlorite, 2.7 for 62% ethanol, and 2.0 for 71% ethanol.[90]

Guidance from the CDC for managing patients with MERS states, "HCP should perform hand hygiene before and after all patient contact, contact with potentially infectious material, and before putting on and upon removal of PPE, including gloves. Hand hygiene in healthcare settings can be performed by washing with soap and water or using alcohol-based hand rubs. If hands are visibly soiled, use soap and water, not alcohol-based handrubs."[91] The CDC further states "Standard cleaning and disinfection procedures (eg, using cleaners and water to pre-clean surfaces prior to applying an EPA-registered disinfectant to frequently touched surfaces or objects for appropriate contact times as indicated on the product's label) are appropriate for MERS-CoV in healthcare settings, including those patient-care areas in which aerosol-generating procedures are performed. If there are no available EPA-registered products that have a label claim for MERS-CoV, products with label claims against human coronaviruses should be used according to label instructions."[91]

CRE

Definition and microbiology

The CDC defines CRE for surveillance purposes as *Enterobacteriaceae* that are "resistant to imipenem, meropenem, doripenem, or ertapenem OR documentation that the isolate possess a carbapenemase."[92] The CDC further elaborates that CRE is "a phenotypic definition (ie, based on the antibiotic susceptibility pattern of the organism) and it includes bacteria that are not susceptible to carbapenems via more than one type of mechanism." The CDC specifies that carbapenem resistance mechanisms include the following: (1) the production of carbapenemases (called carbapenemase-producing-CRE), enzymes that break down carbapenems and related antimicrobials making them ineffective. This includes enzymes like *Klebsiella pneumoniae* carbapenemase; and (2) the combination of mechanisms other than carbapenemase production (called non-carbapenemase-producing-CRE), most commonly the production of β-lactamases (eg, AmpC) in combination with alterations in the bacteria's cell membrane (eg, porin mutations). The CDC has reported the following types of CRE in the United States: NDM, OXA48, VIM, IMP, and *Klebsiella pneumoniae* carbapenemase.[93]

Epidemiology and transmission

The biology, epidemiology, and management of CRE have been reviewed.[94-97] Recent articles have reviewed newer antibiotic therapies for CRE.[98,99] Follow-up of hospitalized CRE colonized patients demonstrated that the mean duration of colonic carriage was >1 year.[100] However, HCP are rarely, if ever, colonized. A study of fecal carriage among HCP in a hospital endemic for CRE revealed none of 177 evaluated health care providers were colonized with CRE.[101]

The main reservoir leading to human CRE infections is the human gut. Person-to-person transmission via direct and indirect contact are the most common mechanisms of transmission (Table 3). Multiple hospital outbreaks have resulted from contaminated endoscopes, especially duodenoscopes.[102-104] These outbreaks have occurred despite all steps in cleaning and high-level disinfection of endoscopes compliant with current guidelines. Strategies to provide pathogen-free endoscopes have been reviewed.[104] Water sources in the hospital (eg, faucets, wash basins, showers, toilets), especially sinks have been demonstrated to be a reservoir of CRE.[105-107] Strategies and success rates of interventions to eliminate CRE from water reservoirs have been reviewed.[105,106] Companion animals have been demonstrated to occasionally be colonized with CRE.[108] This is of relevance to health care facilities considering that US health care facilities must permit persons with "service" animals in the facility and many hospitals permit animal-assisted therapy.

Strategies to manage CRE colonized/infected patients and to control outbreaks in health care facilities have been reviewed.[109-111] Both the WHO[112] and the CDC[113] provide detailed guidance on methods to control CRE. The use of bundles to control horizontal transmission of CRE in health care facilities have been reviewed.[114]

Environmental contamination and survival

CRE has been isolated from the environment in the vicinity of hospitalized colonized/infected patients including pillows, infusion pumps, bedside tables, and toilet areas.[115-117] The frequency of recovery has varied among studies, but objects closer to the patient are more likely contaminated with 5%-15% of samples from bedrails and over bed tables yielding CRE.[115,116] Fecal continence is an

Table 3
Modes of transmission and reservoirs of carbapenem-resistant *Enterobacteriaceae*

- Patient-to-patient via direct contact
- Patient-to-patient via indirect contact
  - Transient hand carriage by health care personnel
  - Contaminated shared medical devices
  - Contaminated endoscopes (especially duodenoscopes)
- Health care facility reservoir to patient
  - Contaminated sinks
  - Contaminated endoscopes (especially duodenoscopes)

independent predictor of being a nonspreader of CRE.[117] CRE has also been isolated in the environment of long-term care facilities.[118]

Havill et al[119] reported survival of CRE on stainless steel discs for >10 days. However, Weber et al[120] reported that 3 species of CRE (*Klebsiella, Enterobacter, and Escherichia coli)* survived poorly (>85% die-off in 24 hours). Likely this difference was owing to the fact that Havill et al[119] used a high inoculum (ie, 5-7-$\log_{10}$) whereas Weber used a low inoculum (ie, ~2-$\log_{10}$), which is similar to the actual amount of CRE found on surfaces in the vicinity of patients colonized/infected with CRE.

Susceptibility to germicides

With rare possible exceptions, antibiotic-resistant bacteria including multidrug-resistant organisms do not have reduced susceptibility to EPA-registered germicides.[121] Even when reduced susceptibility to a germicide (eg, quaternary ammonium compounds by methicillin-resistant *Staphylococcus aureus* [MRSA]) has been demonstrated, the pathogen has not demonstrated resistance to the use concentration of the germicide.[121] Kanamori et al[122] assessed the efficacy of 21 germicides against multiple CRE *Enterobacteriaceae* strains at 1-minute contact time and in the presence of 5% fetal calf serum. Four high-level disinfectants achieved >4-$\log_{10}$ kill for all tested strains, but 0.55% ortho-phthalaldehyde achieved a 2.4-4.8-$\log_{10}$ kill depending on the CRE strain tested. Eight disinfectants all achieved a >4-$\log_{10}$ kill. Among the 9 antiseptics tested (70% ethanol, 10% povidone-iodine, 2% and 4% chlorhexidine gluconate, 70% isopropyl alcohol, and 1% chloroxylenol) achieved ≥2.9-$\log_{10}$ kill against all test CRE strains. Based on this study, EPA-registered disinfectants and FDA-approved antiseptics can be used with assurance for equipment/instrument high-level disinfection, surface disinfection, and hand antisepsis. A UV-C device for room disinfection has been shown to inactivate >5-$\log_{10}$ CRE reduction in direct line of sight and >4-$\log_{10}$ CRE reduction in indirect line of sight when used at the recommended cycle time (ie, 5-10 minutes).[123] The effectiveness of UV-C for room disinfection was confirmed in another study.[124]

C AURIS

History and microbiology

C auris is a novel *Candida* species that was first reported following its isolation from the ear canal of a patient in Japan in 2009.[125] Since then, *C auris* has been reported from multiple countries throughout the world.[126-128] The CDC reported that as of January 22, 2019, 551 cases of *C auris* had been reported from 12 states, with some states (ie, New York, Illinois, New Jersey) reporting >100 cases.[129] *C auris* is an emerging pathogen that presents a serious global health threat for the following reasons: (1) it causes serious infections with a high mortality; (2) it is often difficult to identify with standard laboratory methods and can be misidentified in laboratories unless specialized technology is used; (3) it is often multidrug resistant (intrinsic or rapidly inducible antifungal resistance); (4) it is becoming more widespread geographically; (5) increasing prevalence; (6) biofilm formation; (7) persistence in the environment; and (8) it has caused multiple outbreaks in health care facilities.[128,130,131]

The microbiology, clinical syndromes, diagnosis, and treatment of *C auris* have been reviewed.[127,132-136] Genetic analyses have shown that *C auris* is most closely related to *C lusitaniae* and *C haemulonii*, although it has a striking divergence from some other *Candida* species.[127] *C auris* is often misidentified in conventional diagnostic laboratories using biochemical typing.[127] *C auris* most commonly has been misidentified as *C haemulonii*, but also as *C famata*, *C sake*, *Rhodotorula glutinis*, *R mucilaginosa*, and *Saccharomyces boulardii*.[127,137,138] Currently, accurate identification of *C auris* can be accomplished by the use of MALDI-TOF or PCR assays specific for *C auris*. Multiple virulence factors have been described.[133]

The most common clinical syndromes reported have been bloodstream infections (candidemia), wound infections, and ear infections.[129] Other clinical syndromes reported have included infections of the respiratory tract, central nervous system, urogenital system, intra-abdominal, skin and soft tissues, and bone.[127] Patients with *C auris* infection have almost always presented with underlying illnesses or comorbidities such as diabetes, chronic or acute renal failure, pulmonary disease, immunosuppressive conditions, tumor or malignancies, liver disease, or solid organ transplants.[137] Risk factors for infection have usually included care in an intensive care unit, the presence of indwelling central venous catheters, arterial lines, Foley catheters, invasive surgical procedures, mechanical ventilation, and prior or continued exposure to broad-spectrum antibiotics and antifungal agents.[132,133,136] Mortality rates >30% have been reported for patients with invasive infections.[127,132,133]

At the present time, there are no clinical breakpoints for *C auris*. High minimum inhibitory concentrations have been reported to fluconazole and other triazole antifungals such as voriconazole, itraconazole, and isavaconazole.[127,132] Variability in susceptibility of isolates has also been reported to amphotericin.[127]

Epidemiology and transmission

C auris has been associated with multiple nosocomial outbreaks, especially in the intensive care setting.[139-144] An evaluation of *C auris* in New York City health care facilities demonstrated epidemiologic links between cases in multiple hospitals and long-term care facilities.[138] Importantly, colonization with *C auris* has been detected at multiple body sites including nares, groin, axilla, and rectum.[127] Prolonged colonization has been reported with *C auris* detected >3 months after initial isolation and despite multiple negative screens and antifungal therapy.[136,138]

Multiple mechanisms for transmission of *C auris* are likely based on outbreak investigations (Table 4). Risk factors for colonization or infection have been reported to include contact with patients known to harbor *C auris*.[138,145] Sharing an environment with a *C auris* patient or sequential bed occupancy that was previously occupied by a patient with *C auris* has also been described as a risk.[145] Importantly, patients occupying a room that previously housed a patient with *C auris* have acquired *C auris* even though the room had been decontaminated prior to occupancy.[145] An outbreak evaluation found that use of reusable probes for temperature monitoring was associated with a significantly increased risk of *C auris* colonization with an odds ratio of 6.80.[142] Transmission of *C auris* via transplantation of lung from a patient with respiratory tract colonization or infection to the lung transplant recipient has been reported.[146]

C auris has occasionally been isolated from health care providers. Biswal et al[144] reported that *C auris* was detected on the hands of 4

Table 4
Modes of transmission of *Candida auris*

Common
• Patient-to-patient via direct contact
• Patient-to-patient via indirect contact due to environmental contamination (ie, sharing same hospital room, admission to a hospital room previously occupied by a patient with *C auris*)
Less Common
• Patient-to-patient via indirect contact: shared equipment due to inadequate disinfection (eg, thermometer)
• Patient-to-patient via direct contact: donor-derived transmission (eg, lung transplantation)
• Person-to-person via indirect contact due to transiently colonized health care provider's hands

health care providers (2.8%), although this was likely due to inadequate hand hygiene rather than long-term colonization. Schelenz et al,[139] while conducting an outbreak investigation in the United Kingdom, screened (nose, axilla, groin, and throat) >250 health care providers for colonization and found only a single person (nurse) transiently colonized with *C auris*.

Environmental contamination and survival

Widespread contamination of the surface environment has been reported by multiple investigators.[138] Importantly, contaminated sites have included sites in the patient's room such as surfaces, toilets, ventilator/respiratory equipment, and sites outside of the patient's room such as computer workstations, thermometers, glucometers, housekeeping carts, dialysis equipment, ultrasound equipment, and vital sign machines.[138] The environmental survival of *C auris* has been studied.[144,147,148] In laboratory tests, *C auris* and other *Candida* spp were demonstrated to persist for 7 days on moist or dry (steel disks) surfaces.[147] Survival on dry linen for up to 7 days has been demonstrated.[148] *C auris* cells have been demonstrated to remain viable on plastic surfaces for at least 4 weeks, or 2 weeks after they were no longer culturable.[148]

Susceptibility to germicides

Several reviews have included a discussion of the susceptibility of *C auris* to germicides.[149] The susceptibility of *C auris* to germicides (ie, antiseptics and disinfectants) has been studied by several investigators.[139,144,150-153] Rutala et al[153] assessed the germicidal activity of high-level disinfectants and/or chemical sterilants and reported that all agents (ie, 0.20% peracetic acid, 2.4% glutaraldehyde, 0.65% hydrogen peroxide plus 0.14% peroxyacetic acid, 2% accelerated hydrogen peroxide) achieved a ≥4.1-$\log_{10}$ reduction of *C auris* with the exception of 0.55% ortho- phthalaldehyde that achieved only a 2.3-$\log_{10}$ inactivation for *E coli*. Importantly, these in vitro experiments were done under challenging conditions (ie, 5% fetal calf serum and 1-minute exposure time). It is likely that all high-level disinfectants that are currently approved by the FDA when used appropriately (ie, after appropriate cleaning and the manufacturer's recommended concentration and duration) are effective against *C. auris*.

The activity of low-level disinfectants has been evaluated by several investigations.[152,153] Direct comparison between the studies is impeded by the use of different test conditions including test method, duration of exposure, and presence or absence of proteins such as fetal calf serum. The activity of low-level disinfectants has been most comprehensively investigated using the disc-based quantitative carrier test and is summarized in Table 5.[152,153] Importantly, both investigators added 5% fetal calf serum to assess germicidal efficacy under more stringent conditions (ie, presence of proteins). Importantly, quaternary ammonium disinfectants alone were significantly less effective against *C auris* than other products.[152,153] Some investigators reported that concentrations of sodium hypochlorite ≥1,000 ppm were effective in killing >4-$\log_{10}$ *C auris* in 3-5 minutes,[150,151] whereas others[153] reported sodium hypochlorite ~1,200 ppm at an exposure time of 1 minute resulted in only a 1.6-$\log_{10}$ reduction in *C auris*. It is unclear whether the longer exposure times and lack of protein load led to the high reduction rates reported by Abdolrasouli et al[150] and Moore et al.[151] However, all investigators have reported that a 1:10 dilution of 5.25% sodium hypochlorite is effective in killing >4-$\log_{10}$ *C auris* even with short exposure times (ie, 1 minute) and in the presence of protein.[152,153] Based on current studies, the CDC states "Quaternary ammonium compounds (QACs) that are routinely used for disinfection may not be effective against *C auris*. . ..Until further information is available for *C auris*, CDC recommends use of an Environmental Protection Agency (EPA)-registered hospital-grade disinfectant effective against *Clostridium difficile* spores (List K)".[154] CDC further states that when the use of products on List K is not feasible, published research has found that the following products led to a substantial reduction

Table 5
Susceptibility of *Candida auris* to low-level disinfectants used for surface disinfection*

Highly Effective (≥3.8-$\log_{10}$ Reduction) [ET, minutes]	Moderately Effective (2.0-3.8-$\log_{10}$ Reduction) [ET, minutes]	Less Effective (<2.0-$\log_{10}$ Reduction) [ET, minutes]
• 70% isopropyl alcohol [1] • 1:10 dilution, 5.25% sodium hypochlorite (~6,100-6,700 ppm) [1] • 1:128 dilution, 9.09% o-phenylphenol, 7.66% p-tertiary amylphenol [1] • 1.4% hydrogen peroxide [1] • 58% ethanol, 0.1% QAC† [1] • 55% isopropyl alcohol, 0.5% QAC‡ [1] • 28.7% isopropyl alcohol, 27.3% ethyl alcohol, 0.61% QAC§ [1] • 0.65% sodium hypochlorite [1] • 0.39% sodium hypochlorite [1] • 0.825% sodium hypochlorite [1] • Peracetic acid 1200 ppm, hydrogen peroxide <1%, acetic acid [3] • 1.4% hydrogen peroxide [1] • 0.5% hydrogen peroxide [10] • 29.4% ethyl alcohol [0.5]	• >5% acetic acid (pH 2.0) (white distilled vinegar) [3]	• 1:50 dilution, 5.25% sodium hypochlorite (~1,245 ppm) [1] • 1:256 dilution, 21.7% QAC‖ [1] • QAC¶ [1] • QAC# [1]

NOTE. Susceptibility of *Candida auris* to low-level disinfectants used for surface disinfection.[152,153]
ET, exposure time; *ppm*, parts per million; *QAC*, quaternary ammonium compound.
*Disc-based quantitative carrier test, 1 minute exposure time unless otherwise noted, 5% fetal calf serum.
†QAC: alkyl (C14 50%, C12 40%, C16 10%) dimethyl benzyl ammonium saccharinate 0.1%.
‡QAC: n-alkyl (C12 68%, C14 32%) dimethyl ethylbenzyl ammonium chlorides 0.25%; n-alkyl (C14 60%, C16 30%, C12 5%, C18 5%) dimethyl benzyl ammonium chlorides 0.25%.
§QAC: didecyl dimethyl ammonium chloride 0.61%.
‖QAC: octyl decyl dimethyl ammonium chloride 6.51%; dioctyl dimethyl ammonium chloride 2.604%; didecyl dimethyl ammonium chloride 3.906%; alkyl (50% C14, 40% C12, 10% C16) dimethyl benzyl ammonium chloride 8.68%.
¶Alkyl dimethyl benzyl ammonium chlorides.
#Didecyl dimethyl ammonium chloride, n-alkyl dimethyl benzyl ammonium chloride.

Table 6
Susceptibility of *Candida auris* to antiseptics in selected studies*

Disinfectant	Log_{10} Reduction (minutes)	Reference
Alcohol		
70% alcohol	6.0 (NS)	Biswal et al, 2017[144] †
70% ethanol	4.0 (1)‡	Rutala et al, 2019[153]
70% isopropanol	3.8 (1)‡	Rutala et al, 2019[153]
CHG		
0.5%	6.0 (NS)	Biswal et al, 2017[144]
2.0%	1.6 (1)‡	Rutala et al, 2019[153]
4.0%	1.9 (1)‡	Rutala et al, 2019[153]
CHG/alcohol		
2% CHG/61% ethanol	>5.06 (2)	Moore et al, 2017[151]
1% CHG/61% ethanol	2.0 (1)‡	Rutala et al, 2019[153]
Povidone-Iodine		
10%	>4.56 (2)	Moore et al, 2017[151]
10%	2.5 (1)‡	Rutala et al, 2019[153]
Triclosan		
0.5%	1.4 (1)‡	Rutala et al, 2019[153]
Hydrogen peroxide		
3.0%	1.4 (1)‡	Rutala et al, 2019[153]
Chloroxylenol		
1%	2.8 (1)‡	Rutala et al, 2019[153]

CHG, chlorhexidine gluconate; *NS*, not stated.
*All tests were conducted in vitro unless otherwise noted.
†Human challenge study.
‡Test conditions included addition of 5% fetal calf serum.

(>4-log_{10}) of *C auris* in laboratory testing: Oxivir TB (Diversey Inc., Charlotte, NC), Clorox Healthcare Hydrogen Peroxide Cleaner Disinfectant (Clorox, Oakland, CA), Prime Sani-Cloth Wipe (PDI, Inc., Woodcliff, NJ), and Super Sani-Cloth Wipe (PDI, Inc., Woodcliff, NJ).[154]

Room disinfection with a UV-C device has been investigated for its ability to inactivate *Candida* spp, MRSA, and *Clos difficile*.[155] *C auris* demonstrated substantially less susceptibility to UV-C than MRSA and less susceptibility than *C albicans* or *C glabrata* at 10 minutes exposure time.[155] Reductions in *C auris* and *Clos difficile* were similar at 10 minutes.[155] With regard to room disinfection devices, the CDC states that "data on hands-free disinfection methods, like germicidal UV irradiation, are limited, and these methods may require cycle times similar to those used to inactivate bacterial spores (eg, *Clostridium difficile*) when used for *C auris*."[154] We recommend that daily and terminal room cleaning/disinfection be done with an agent demonstrated to be effective against *C auris*. The use of a UV-C device for terminal disinfection should be considered as a supplemental method.

The activity of antiseptics against *C auris* has been studied by several investigators (Table 6). There is good agreement that 70% alcohol (both isopropyl and ethyl) is effective against *C auris* at 1 minute. Importantly, the activity of alcohol has not been studied at the times used by most health care providers when performing hand hygiene (ie, 10-15 seconds). Unfortunately, studies on the activity of other important antiseptics such as chlorhexidine gluconate and povidone-iodine have produced variable results (Table 6). This variability is likely explained by differences in the test conditions including in vitro versus human challenge, duration of exposure, and presence of a protein load (eg, fetal calf serum). It appears that 10% povidone-iodine would provide adequate skin antisepsis if applied for ≥1 minute. Using a panel of *C auris* clinical isolates, Kean et al,[156] screened them for their planktonic and sessile susceptibilities to skin disinfection challenge using povidone-iodine, chlorhexidine gluconate, and hydrogen peroxide. *C auris* biofilms displayed increased tolerance to antisepsis compared with planktonic cells. Analysis using a complex biofilm model demonstrated reduced susceptibility against clinically relevant concentrations of chlorhexidine gluconate (0.05%) and hydrogen peroxide (3%), with eradication achieved only with povidone-iodine (10%). As noted by Forsberg et al,[136] whether topical antiseptics might reduce the burden of *C auris* on the skin, and therefore provide a potentially valuable tool for infection prevention, remains unclear. The CDC states that when caring for patients with *C auris* "healthcare personnel should follow standard hand hygiene practices, which include alcohol-based hand sanitizer use or, if hands are visibly soiled, washing with soap and water. Wearing gloves is not a substitute for hand hygiene."[154]

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