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SPECIAL REPORT

Emerging Pathogens and Environmental Cleaning

This report examines surface cleaning and disinfection in the face of emerging infectious disease and the pathogens that can challenge disinfectant efficacy. It reviews the hierarchy of pathogen resistance and susceptibility to disinfectants, discusses various factors that impact disinfectant efficacy, and addresses current pathogens of concern.

By Kelly M. Pyrek

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Emerging infectious diseases (EIDs) pose a challenge to institutions in terms of being prepared for how to clean and disinfect the healthcare setting when a patient has a known or suspected infection with an emergent pathogen. While existing guidance may not necessarily be keeping up with these EIDs, infection preventionists and environmental services professionals should be able to cope by breaking down the etiology of the pathogen in question, consulting what is known in the existing guidelines and medical literature, and proceeding accordingly.

Bacteria and viruses vary in their susceptibility and resistance to disinfectants and their ability to be inactivated. Klein and Deforest classified viral groups according to the least resistance to disinfectants (the enveloped viruses such as influenza, coronavirus and Ebola), to those with moderate resistance (such as the large non-enveloped viruses like adenovirus), to those with the most resistance to disinfectants (the small non-enveloped viruses such as piconavirus and parvovirus). Noll and Youngner classified viruses in three groups: category A: most susceptible to disinfectants (viruses that have lipoprotein envelopes); category B: least susceptible to disinfectants, small non-enveloped viruses; and category C: intermediate susceptibility to disinfectants, the large non-enveloped viruses.

A widely accepted hierarchy of microbial resistance to disinfectants and sterilants (listed from the most resistant to the most susceptible), modified from McDonnell and Burke by Rutala and Weber (2014) is as follows:

- Prions (such as Creutzfeldt-Jakob disease agent)
- Bacterial spores (such as Clostridium difficile)
- Protozoan oocytesa (such as Cryptosporidium)
- Helminth eggsa
- Mycobacteria (such as Mycobacterium tuberculosis)
- Small, nonenveloped viruses (such as poliovirus, parvovirus, papilloma virus, norovirus)
- Protozoal cystsa (such as Giardia)
- Fungal spores (such as Aspergillus, Penicillium)
- Gram-negative bacteria (such as Pseudomonas, Escherichia)
- Vegetative fungi and algae (such as Aspergillus, Candida)
- Vegetative helminthes and protozoaa (such as Giardia)
- Large, nonenveloped viruses Adenovirus, rotavirus
- Gram-positive bacteria (such as Staphylococcus, Enterococcus)
- Enveloped viruses (such as herpes, influenza, HIV, HBV)

> In terms of resistance to biocides, mammalian viruses are mainly divided into two types, enveloped viruses and non-enveloped viruses."
>
> **—Sakudo, et al. (2010)**

Sakudo, et al. (2010) remind us that "A virus is a particle composed of nucleic acids surrounded by proteins. Viruses cannot survive and multiply without host cells because they cannot produce energy by themselves. Viruses include bacteriophages, which infect bacteria." They add, "In terms of resistance to biocides, mammalian viruses are mainly divided into two types, enveloped viruses and non-enveloped viruses. Enveloped viruses, which include human immunodeficiency virus (HIV), hepatitis B virus (HBV), influenza viruses, and herpes simplex virus (HSV), are considered more sensitive to biocides. Their characteristics depend on structure including the external lipid bilayer envelope, which contains proteins (usually glycoproteins, or proteins with linked carbohydrate groups). The infectious unit of a virus is the virion, envelope + nucleocapsid. Enveloped viruses are easily destroyed by agents affecting lipids such as alcohols, ether, 2- phenlphenol, cationic surfactants, and chlorhexidine. Studies have shown that disinfection with alkaline glutaraldehyde (2%) effectively destroys the hepatitis C virus (HCV), HBV and HIV. HIV can be inactivated by 70% isopropanol + 0.5% chlorhexidine gluconate (CHG), 40% CHG, chloroxylenol, and benzalkonium chloride. In contrast, non-enveloped viruses, which include the norovirus, poliovirus, and human hepatitis A virus (HAV), are composed of a nucleocapsid without an envelope. In these viruses, the virion is the nucleocapsid itself. Non-enveloped viruses are more resistant than enveloped viruses and not inactivated by alcohols. However, several reports have suggested that alcohols at high concentrations reduce the viral titers of relatively large non-enveloped viruses such as rotavirus, adenovirus, rhinovirus and hepatitis A virus (HAV). The resistance of small non-enveloped viruses is generally greater than that of Gram-positive and Gram-negative bacteria and vegetative fungi."

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— Sakudo, et al. (2010)

Sakudo, et al. (2010) point to the recent emergence and re-emergence of pathogens that represent a threat to public health: "Studies have proven that most of these pathogens, with the exception of prions, HPV and norovirus, are sensitive to commercial disinfectants. Although outbreaks of rotavirus-caused gastroenteritis have been reported in pediatric clinics, agents confirmed to be effective against rotavirus include 95% ethanol, 70% isopropanol, 2% glutaraldehyde, 0.35% peraceutic acid, phenol, and quaternary ammonium. SARS coronavirus is completely inactivated by treatment with 70% ethanol + povidone iodide, 2.5% glutaraldehyde. There are no reports on the disinfection of human papillomavirus (HPV) and norovirus, neither of which can be made to proliferate in vitro using current technologies, although both viruses are very important for public health. A substitute for norovirus is the feline calicivirus (FCV), which is a related species and can proliferate in vitro. Bleaching agent (1,000 ppm), accelerated hydrogen peroxide (5,000 ppm), chlorine disinfectant (1,000 ppm), chlorine dioxide, quaternary ammonium (2,470 ppm), 0.1% quaternary ammonium + 79% ethanol, and 75% ethanol are all effective in inactivating FCV. Reagents such as glutaldehyde, hypochlorite, phenol, ethylene oxide and hydrogen peroxide, and treatments such as ultraviolet (UV) light, radiation, and heating have a broad spectrum of effect for the

inactivation of viruses. Such treatments attack DNA, RNA, proteins, and/or lipids and affect the nucleocapsid complex. As the nucleocapsid complex is the basic structural unit of viruses, its destruction causes a reduction in infectivity even in non-enveloped viruses. However, the effectiveness of heating varies possibly due to the secondary and tertiary structure of viral capsid proteins. Therefore, confirmation of the effectiveness of each disinfectant against viruses using a reliable standardized system is required."

Researchers caution that the classification of viruses — either based on genome composition or envelope/non-envelope structures — may not provide a foolproof prediction of disinfection efficacy. For example, Sigstam, et al. (2013) demonstrated that even a subtle change in the genome composition of closely related viruses can yield up to 44 times difference in disinfection kinetics, while Meyers, et al. (2014) found that a virus surrogate has shown distinct disinfection efficacy. Hambidge (2001) indicated that organic matter can significantly affect a disinfectant's efficacy either by reducing the effective concentration or by protecting viral particles from detrimental effect. This is particularly relevant in the hospital environment when contamination may be associated with blood, serum, soil, feces and other organic materials. (See section on Disinfectants)

Rutala and Weber (2014) echo this caution, pointing out that "The traditional hierarchy developed by Spaulding is still widely used but is based on disinfectant knowledge from 1957. Today, our understanding of the resistance profiles of pathogens (e.g., viruses, protozoans, spores) by disinfectants is more informed; however, it is important to recognize that this hierarchical scale is only a guide to microbial susceptibility of pathogens to disinfectants, and it may vary depending on the type of microorganisms, how they are presented for disinfection (e.g., in suspension or dry on carrier), the test method (e.g., quantitative carrier tests), and the active ingredient and how it is formulated (e.g., surfactants, chelating agents). For example, for non-sporicidal disinfectant formulas, mycobacteria (marker strains Mycobacterium bovis or Mycobacterium terrae) are considered the most resistant vegetative bacteria. However, while alcohols can inactivate mycobacteria, they are less active against small, non-enveloped viruses, such as poliovirus. This means that a product EPA registered to kill M. tuberculosis with a 1-minute contact time may not be capable of inactivating other pathogens traditionally considered to be 'more susceptible' (such as poliovirus and norovirus) within the 1-minute time frame. Because of the variation in the susceptibility of microorganisms to disinfectants, users should check disinfecting labels for the relevant kill claims (those that cause most HAIs and outbreaks) in addition to considering the historically accepted hierarchy model."

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— Rutala and Weber (2014)

Disinfectants

Reichel, et al. (2014) remind us of the simple guidelines regarding disinfectant efficacy: "Targeted surface disinfection is a major measure of standard infection control. The surface disinfectants must be effective against the targeted pathogens. Surfaces near patients and high-touch surfaces must be effectively disinfected."

Disinfectants can act on microorganisms in two different ways: growth inhibition (bacteriostasis, fungistasis) or lethal action (bactericidal, fungicidal or virucidal effects). Maris (1995) indicates that "there may be considerable variation (in terms of pH, hardness, salinity, etc.) in the media surrounding the target microorganisms, and the state in which the latter is present (e.g., bacterium isolated or included in complex biofilm). Understanding the mode of action of disinfectants requires an examination of the structure and functions of the bacterial cell."

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Maris (1995) explains that a disinfectant can act on pathogens in several ways:

- It acts on the external membrane of the bacterial wall
- It acts on the bacterial wall itself
- It acts on the cytoplasmic membrane
- It acts on the pathogen's energy metabolism (some disinfectants act on ATP production)
- It acts on the cytoplasm and nucleus at the chromosome level

Action on bacterial spores should be noted. As Maris (1995) observes, "The impermeability and the presence of dipicolinic acid in bacterial spores make these forms much more resistant to disinfectants than vegetative forms. The active disinfectants include highly oxidizing products, such as hydrogen peroxide and chlorine, which can destabilize this structure in spores."

A number of compounds are used against pathogens in the healthcare setting, including acidic and alkaline compounds; chlorine and derivatives; quaternary ammonium compounds (QACs); phenolic compounds; iodine compounds; iodophors; and hydrogen peroxide, among others.

Rutala and Weber (2014) emphasize that "All disinfectants used in healthcare should be EPA-registered, which can be confirmed on antimicrobial products listings and manufacturer's label claims."

The EPA lists contain disinfectants effective against certain bloodborne/body fluid pathogens to include Mycobacterium tuberculosis, HIV, HBV, hepatitis C virus, and products classified as sterilizers. Listings also include EPA-registered products effective against MRSA, vancomycin-resistant Enterococcus faecalis or Enterococcus faecium (VRE), human norovirus, and C. difficile spores. The lists are organized alphabetically by product name and by numerical order of their EPA registration number and can be found at:

http://www.epa.gov/oppad001/chemregindex.htm).

Rutala and Weber (2014) explain that there are three types of disinfectant products that

are EPA-registered on the basis of submitted efficacy data: limited, general or broad-spectrum, and hospital disinfectants: "When a disinfectant is represented in its labeling for use in hospitals (i.e., hospital disinfectant), medical clinics, dental offices, or any other medical-related facility, it must show effectiveness against two Gram-negative microorganisms (Salmonella choleraesuis ATCC 10708, P. aeruginosa) and one Gram-positive microorganism (S. aureus ATCC 6538). In addition to the efficacy data for a public health claim, the applicant is required to submit supporting data pertaining to product chemistry and toxicologic hazards."

Rutala and Weber (2014) add that EPA testing does not mimic real-world situations: "Product testing for the EPA requires testing under hard-water conditions (e.g., up to 400-ppm hardness, CaCO3) in the presence of 5 percent serum concentration to simulate the product's effectiveness under in-use conditions. Some of the issues associated with current testing that have been raised include unrealistic contact times (10 minutes is too long for hospital use), long lists of irrelevant organisms on product labels (e.g., many spread primarily by methods other than contaminated environmental surfaces), soil load (e.g., a standardized level of soil should be added to the disinfectant test), test methodology (e.g., suspension vs carrier tests), composition of test surface (e.g., glass, stainless steel, Formica), testing does not include physical removal (e.g., label claims for disinfectants based on tests that do not include wiping), and product volume to surface area (e.g., wet-contact time)."

There are a number of factors to take into consideration when using disinfectants:

- Survival of pathogens on inanimate surfaces. As Rutala and Weber (2014) note, "Survival of pathogens on environmental surfaces is critical to the potential of that surface to act as a reservoir or source of the pathogen. There are many factors that determine the survival of pathogens on inanimate surfaces as well as their transfer to other surfaces; the factors include temperature, relative humidity, topography, porosity, suspending medium, higher inocula, duration of contact, surface material (e.g., plastic, steel), other microbes, biofilms, product volume to surface area, type of microbe, disinfectant residual, microbial load, and contacting surface (e.g., bare hands or gloves)."
- Wet contact time. As Rutala and Weber (2014) explain, "Each disinfectant requires a specific length of time it must remain in contact with a microorganism to achieve complete disinfection. This is known as the kill time (or contact time), and kill times for each microorganism will be listed clearly on the label of EPA-registered disinfectants. Fast kill times are important because they give you confidence that you are killing the prevalent and most common healthcare-associated pathogens before the disinfecting solution can dry or be removed and before patients or staff are likely to retouch the surface. Ideally, the contact time should be greater than or equal to the kill time."
- Pathogens dictate contact time. As Rutala and Weber (2014) point out, "Another issue is which pathogen on the disinfectant label should be used to identify contact time (e.g., bacteria, Candida, mycobacteria, spores) for surfaces in healthcare facilities. The Centers for Disease Control and Prevention guideline based the minimum 1-minute contact time for disinfection of noncritical surfaces on demonstration of

bactericidal activity for vegetative bacteria, such as S. aureus, Enterococcus, E. coli, coagulase-negative Staphylococcus, P. aeruginosa, Klebsiella species, Enterobacter species, and so on. These vegetative bacteria are the pathogens that cause the vast majority of HAIs (approximately 80 percent). Furthermore, contaminated surfaces with organisms such as Candida, nontuberculous mycobacteria, and other fungi have rarely been shown to be a risk factor for HAIs. The only exception to this principle of low-level disinfectants for at least 1 minute on environmental surfaces is the use of EPA-registered disinfectant effective against C. difficile spores or norovirus for disinfecting the rooms of patients with one of these pathogens (see http://www.epa.gov/oppad001/chemregindex.htm)."

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Amount of disinfectant left on the surface. This is critical because it affects the contact time and the concentration of active ingredients delivered to the surface. As Rutala and Weber (2014) explain, "Below a certain amount of liquid per surface area, the desired antimicrobial affect will not be achieved. Thus, 'damp dusting' using a barely wet cotton cloth or disposable disinfectant wipe will not result in the desired antimicrobial reduction, as the surface was not wetted for the contact time with an appropriate use dilution of the disinfectant. Similarly, results have demonstrated efficient transfer of C. difficile spores from contaminated to clean surfaces by nonsporicidal wipes and overused sporicidal wipes. In contrast, wiping with sporicidal agents eliminated more than 3.90-log10 C. difficile spores by inactivation and/or physical removal."

- Thoroughness of cleaning and disinfecting practices. As Rutala and Weber (2014) emphasize, "while disinfectant wet-contact time is critical for thorough surface disinfection, nothing is more important than the thoroughness of cleaning/disinfecting all hand-contact surfaces (e.g., environmental surfaces or patient-care equipment), as current studies demonstrate that less than 50 percent of high-risk objects are cleaned/disinfected at terminal cleaning. Wiping all hand-contact or touchable surfaces and equipment—and not just perceived high-risk surfaces and equipment—is essential because high-risk surfaces and equipment have not been epidemiologically defined."

Weber, et al. (2010) outline the microbiologic factors that can facilitate surface environment-mediated transmission of selected pathogens:

- Pathogen able to survive for prolonged periods of time on environmental surfaces (all)
- Ability to remain virulent after environmental exposure (all)
- Contamination of the hospital environment frequent (all)
- Ability to colonize patients (Acinetobacter, C difficile, MRSA, VRE)
- Ability to transiently colonize the hands of healthcare workers (all)
- Transmission via the contaminated hands of healthcare workers (all)
- Small inoculating dose (C difficile, norovirus)
- Relative resistance to disinfectants used on environmental surfaces (C difficile, norovirus)

Rutala and Weber (2014) outline the properties of an ideal disinfectant:

1. Broad spectrum. Should have a wide antimicrobial spectrum, including kill claims for the pathogens that are the common causes of HAIs and outbreaks.
2. Fast acting. Should have a rapid kill and short kill/contact time listed on the label.
3. Remains wet. Should keep surfaces wet long enough to meet listed kill/contact times with a single application or meet wet times recommended by evidence-based guidelines.
4. Not affected by environmental factors. Should be active in the presence of organic matter (e.g., blood, sputum, feces) and compatible with soaps, detergents, and other chemicals encountered in use.
5. Nontoxic. Should not be irritating to the user, visitors, and patients. Should not induce allergic symptoms (especially asthma and dermatitis). The toxicity ratings for disinfectants are danger, warning, caution, and none. Ideally, choose products with the lowest toxicity rating.
6. Surface compatibility. Should be proven compatible with common healthcare surfaces and equipment.
7. Persistence. Should have sustained antimicrobial activity or residual antimicrobial effect on the treated surface.
8. Easy to use. Should be available in multiple forms, such as wipes (large and small), sprays, pull tops, and refills; directions for use should be simple and contain information about personal protective equipment as required.
9. Acceptable odor. Should have an odor deemed acceptable by users and patients.
10. Economical. Costs should not be prohibitively high but when considering the costs of a disinfectant one should also consider product capabilities, cost per compliant use, and so on.
11. Solubility. Should be soluble in water.
12. Stability. Should be stable in concentrate and use dilution.
13. Cleaner. Should have good cleaning properties.
14. Nonflammable. Should have a flash point above 150 degreesF.

Source: Modified from Molinari et al. and Rutala and Weber (2014)

Pathogens of Concern

Science and industry are still playing catch-up with certain pathogens. As Rutala and Weber (2014) acknowledge, "Due to the constant evolution of pathogens causing infections, especially emerging pathogens (e.g., Middle East respiratory syndrome coronavirus [MERS-CoV]), a new or emerging pathogen will likely not have an EPA-registered disinfectant on the market to kill it. Manufacturers may not make claims about any emerging pathogen without EPA approval, and it can take 18 to 24 months for a manufacturer to obtain label claims for new pathogens (see http://www.epa.gov/oppad001/disinfection_hier.htm). Until an EPA-approved claim is available, users may need to refer to the hierarchy of microbial susceptibility to select the appropriate disinfectant for the emerging pathogen. If the microbiologic class of a new microbe is established, the class-specific test organism(s) would serve as a surrogate for evaluating disinfectant efficacy. The label claim (i.e., registration) would be based on the use of a validated EPA-approved test that assessed the efficacy of disinfectants against the

class-specific test organism. For example, an EPA claim against poliovirus or hepatitis A virus could be used for MERS-CoV as well as data in peer-reviewed literature that demonstrated inactivation of coronavirus. Until a new or emerging microbe could be placed in a microbiologic class, it is suggested that only disinfectants with a mycobactericidal claim be allowed by the EPA. For example, the severe acute respiratory syndrome agent, prior to isolation and characterization as a coronavirus, would necessitate the use of a disinfectant with a mycobactericidal label claim for surface disinfection. Once the agent is characterized and placed into a microbial class (e.g., as a coronavirus), all EPA products with a label claim against viruses (e.g., test agent, poliovirus) would be acceptable. In the event that there is not a validated test organism in a class, the next most resistant class should be used for purposes of registering disinfectants. For example, if a surrogate for an enveloped virus is not validated, then a small, non-enveloped virus (e.g., poliovirus) could be used instead. Using this accumulated knowledge of microbial susceptibility should discourage unnecessary testing, listing irrelevant organisms on labels, and 'bug-of-the-month' testing."

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"These emerging pathogens are killed by our current hospital-grade disinfectants," says Louise Dembry, MD, MS, MBA, president-elect of SHEA and hospital epidemiologist at Yale-New Haven Hospital. "I am not aware of any evidence that suggests they are 'mutating' in such a way that makes them resistant to the disinfectants commonly used in hospitals. It is important to use the disinfectants correctly and follow the manufacturers' directions (such as contact time which is the amount of the time a surface needs to remain wet with the disinfectant to achieve expected activity). It does not appear that additional steps need to be taken, however it is important to ensure that cleaning/disinfection of surfaces and the environment takes place regularly and possibly more frequent than usual for pathogens such as Ebola where there can be extensive contamination of the environment with blood/body fluids from the patient." Dembry adds, "Low-level disinfection of surfaces and the environment around the patient is adequate but it needs to be done thoroughly and appropriately."

Dembry notes that emerging pathogens are not dictating a new set of game rules for cleaning and disinfection of surfaces at this time. "Organism-specific pathogen environmental disinfection would only add to the confusion," she says. "One would need to know what each patient harbors (not just infection but colonization) and then would there be a combination of protocols to follow should a patient have VRE and influenza? This would require specific protocols for hundreds of organisms that in the end would all be similar protocols, leading to even more staff confusion. Mutating viruses are not usually less susceptible to hospital disinfectants; it may make them more virulent to the host or less susceptible to treatment. ake Ebola for example, it is very easily killed by hospital disinfectants but the cleaning/disinfecting process has to be done correctly for the disinfectants to work – that's the key, not different disinfectants, in my opinion."

Let's take a look at a few EIDs and what is known and recommended for cleaning and disinfection.

Enterovirus D68 (EV-D68)

Enterovirus D68 (EV-D68) is one of many non-polio enteroviruses and is a member of the Picornavirus family of viruses, which are small, non-enveloped RNA viruses. Enterovirus is a common respiratory virus; however, Enterovirus D68 has not been commonly reported since it was first identified in 1962, and in the summer of 2014, it sickened more than 150 people in 18 states. Enterovirus 68 is a large, non-enveloped, single-stranded RNA virus. EV-D68 causes respiratory illness and is transmitted from person to person occurs through coughing, sneezing, or touching of contaminated surfaces. According to the CDC, disinfection of surfaces in healthcare settings should be performed using a hospital-grade disinfectant with an EPA label claim for any of several non-enveloped viruses, such as norovirus, poliovirus or rhinovirus (CDC, 2014). For EV-D68, the CDC recommends hand hygiene as well as cleaning and disinfecting frequently touched surfaces. Manufacturers of disinfectants generally recommend that products suitable for use against EV-D68 should fall within CDC and EPA criteria. Per those criteria, an EPA-registered hospital disinfectant should be used that (1) possesses EPA-registered claims against at least one non-enveloped virus (norovirus, adenovirus, rotavirus, poliovirus, hepatitis A virus); (2) is registered for hard, nonporous surfaces; and (3) has had all its efficacy claims confirmed under the Antimicrobial Testing Program. Such products should be used for the approved use site(s), in accordance with the manufacturer's instructions for the specific disinfection label claim, and in a manner consistent with standard environmental infection control practices. To determine whether EPA has confirmed a product's efficacy, refer to the List of ATP-tested Hospital Sterilants, Disinfectants and Tuberculocides on the EPA website. Evaluation of virus inactivation is a critical component of disinfectant testing. The US Environmental Protection Agency (EPA) considers a disinfectant agent to be effective if the product can demonstrate complete inactivation of the virus at all dilutions while at least 4 logs of virus particles per milliliter must be recovered from the nonvirucidal treated control carrier (EPA, 1981).

Avian influenza virus

Influenza A viruses are constantly changing, and they might adapt over time to infect and spread among humans. There are only three known subtypes of human flu viruses (H1N1, H1N2, H3N2). It is likely that some genetic parts of current human influenza A came from birds originally. Therefore, the H5N1 virus is of greatest concern for human health because the H5N1 virus has caused the greatest number of human cases of severe sickness and the greatest number of deaths, and there is the risk that the H5N1 virus will mutate enough to start a human influenza pandemic.

Avian influenza virus is a lipid-enveloped, negative-sense, single-stranded RNA virus of the family Orthomyxoviridae and genus Influenzavirus A (Swayne and King, 2003). Avian influenza is transmitted horizontally between birds and infected birds can shed large amounts of the virus via aerosol respiratory droplets and feces. Anything coming in contact with respiratory

secretions or feces of infected birds can become contaminated, including poultry house surfaces and farm equipment. To properly control and eradicate virus during an outbreak, it is necessary to effectively disinfect all surfaces contaminated with potentially infectious material. Lipid-enveloped viruses have been found to stay infective on hard, nonporous surfaces, up to 14 days in the case of human immunodeficiency virus.

In their study, Terpstra et al. (2007) looked at five important (model) viruses in a surface-dried state showing persistence of infectivity, resistance to three commonly used disinfectants and restoration of susceptibility after rehydration. The researchers say their results may have implications for hygiene measurements in the prevention of virus transmission. Terpstra, et al. (2007) examined 0.1 N NaOH and 0.1% hypochlorite for their capacity to inactivate surface-dried lipid-enveloped (LE) [human immunodeficiency virus (HIV), bovine viral diarrhea virus (BVDV) and pseudorabies virus (PRV)] and non-lipid-enveloped [NLE; canine parvovirus (CPV) and hepatitis A virus (HAV)] viruses in a background of either plasma or culture medium. In addition, 80% ethanol was tested on surface-dried LE viruses. The researchers note, "Without treatment, surface-dried LE viruses remained infectious for at least one week and NLE viruses for more than one month. Irrespective of the disinfectant, inactivation decreased for viruses dried in plasma, which is more representative of viral contaminated blood than virus in culture medium. Inactivation by all disinfectants improved when preceded by rehydration, although the infectivity of CPV actually increased after rehydration and disinfection may thus be overestimated in the absence of rehydration."

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> **— Louise Dembry, MD, MS, MBA**

Coronaviruses and MERS-CoV

According to Antimicrobial Test Laboratories, two strains of human coronavirus, 229E and OC43, are known to cause approximately 25 percent of colds that exhibit symptoms similar to those caused by the rhinoviruses (e.g. runny nose, sneezing and cough). However, recent zoonotic strains of coronavirus characterized by species-jumping from animals to humans have gained notoriety and become of particular concern over the past decade. The SARS-CoV (Severe Acute Respiratory Syndrome coronavirus) outbreak of 2002-2003 originated in bats and spread indirectly to humans via intermediate animals (e.g. civet cats). According to Hawryluck, et al. (2005), from the earliest reported cases in southern China, the virus eventually spread to 28 countries over the course of eight months; thousands are believed to have been infected and 774 deaths were reported. More recently, the MERS-CoV (Middle East Respiratory Syndrome Coronavirus) outbreak originating in Saudi Arabia in April of 2012 has made headlines due to its high mortality rate of 45 percent and rapid spread to nine countries; clusters of cases have continued to be reported in the Middle East through present day.

Coronaviruses 229E and OC43 are spread from person-to-person by way of contaminat-

ed aerosols. However, the potential for transmission from contaminated fomites remains of concern as demonstrated by the continued viability of strain 229E more than three hours after drying onto porous and non-porous materials including aluminum and sterile sponges; strain OC43 remained infectious up to one hour after drying on the same surfaces (Sizun, et al. 2000). Sattar, et al. (1989)'s study evaluating 16 antimicrobial products found that all achieved 3-log10 reductions of human coronavirus strain 229E dried in the presence of organic soil onto stainless steel disks except for a quaternary ammonium compound, a chlorhexidine gluconate-centrimide product, and a phenolic formulation. In addition, low levels of sodium hypochlorite, chloramine T, and a mixed halide were not effective, although greater concentrations of these actives did reduce strain 229E levels by 3-log10. Antimicrobial Test Laboratories points out that no studies have been published to-date detailing disinfection efficacy nor inactivation rates of MERS-CoV on surfaces nor in fluids. It adds, "Although SARS-CoV appears to be more environmentally resistant relative to the respiratory coronaviruses, its enveloped structure is still vulnerable to a wide range of disinfectants. Suspension evaluations of propanol (100% and 70%) and ethanol (78%) demonstrated reduction of SARS-CoV to levels below detection in 30 seconds; 60 seconds were required for wine vinegar and 120 seconds for formaldehyde (0.7% and 1%) and 0.5% glutardialdehyde (Rabenau, et al. (2005). Povidone-iodine (PVP-I) products, quaternary ammonium compounds, free chlorine, and catalytic oxidation via Ag/Al2O3 and Cu/Al2O3 active surfaces have also been proven to completely inactivate SARS-CoV. Therefore, environmental transmission of coronaviruses via fomites and liquids can be minimized given the proper implementation of disinfection protocols."

Geller, et al. (2012) notes that "From November 2002 to July 2003, SARS-CoV affected more than 8,000 people in all five continents and caused about 800 deaths. One of the striking features of this epidemic was its nosocomial propagation and the heavy burden of the healthcare workers. Moreover, the mortality rate was higher than 50% in aged (>60-year-old) populations. SARS-CoV seemed predominantly transmitted by respiratory droplets over a relatively close distance. However, direct and indirect contact with respiratory secretions, feces or animal vectors could also lead to transmission, at least under some circumstances. Besides these pathogenic properties, coronaviruses represent another risk for human population through their interspecies jumping capacity. The SARS-CoV is a zoonotic virus that crossed the species barrier. Phylogenetic analysis of SARS-CoV isolates from animals and humans strongly suggest that the virus originated from animals, most likely bats, was amplified in palm civets, and transmitted to human population via live animal markets. This potency of coronaviruses may be responsible for new disastrous outbreaks and therefore should be kept in mind."

Geller, et al. (2012) emphasize that while HCoVs are enveloped, but they are not that fragile, and that they have the potential for virus transfer and cross-contamination: "Indeed, despite the fact that transmission was believed to be mainly achieved by direct physical contact with infected patient or by respiratory droplets, several well-described clusters of infection were difficult to explain by these routes. Examples include transmission to 22 persons on an aircraft, to 13 guests sharing the same floor of a hotel, and more than 300 persons in an apartment complex. These observations led to some speculations about a possible trans-

mission by other means including surfaces, hands, etc., and to the study of SARS-CoV (and other HCoVs) survival in different conditions."

It is crucial to remember that coronaviruses survive well in suspension, and that desiccation has a more severe effect on coronaviruses. Geller, et al. (2012) report that in standard environmental conditions (21 °C and 50% to 70% of relative humidity), HCoV 229E infectivity came down to 30 percent after three hours of desiccation on various surfaces that can be found in hospital settings, such as aluminum, sterile sponges or surgical latex gloves. Rabenau, et al. (2005) found that the infectious titer of SARS-CoV was stable over nine days, with and without proteins. After drying on a plastic surface, the HCoV 229E and the HSV-1 lost their infectivity in 72 hours, in the presence or absence of FCS. In contrast, the SARS-CoV retained its infectivity for as long as six days, with a further protecting effect of proteins. It took nine days in a dried state, for SARS-CoV to completely lose its infectivity. The adenovirus was the most stable virus assayed as it conserved its infectivity throughout the nine days of the experiment. Other studies (Duan, et al.; Sizun, et al.; and Lai, et al.) confirm these results. SARS-CoV has been shown to survive after drying on different kinds of materials or diluted in water, revealing a decreased infectivity only after 72 to 96 hours, depending on the conditions. However, its infectivity is reduced more rapidly if it is deposited on porous surfaces such as cotton or paper.

> "One of the striking features of [the SARS] epidemic was its nosocomial propagation and the heavy burden of the healthcare workers."
>
> **— Geller, et al. (2012)**

Geller, et al. (2012) conclude that "Besides the absence of specific treatment and vaccine, HCoVs are now known to show a significant environmental resistance. Their survival in different biological fluids such as respiratory secretions or feces has been proved. Furthermore, some parameters seem of benefit for HCoVs such as the stabilizing effect of low temperature and high relative humidity or the protective action of organic materials. This protective effect should be carefully considered when developing antiseptic-disinfection strategies. Indeed, this often involves a higher quantity and/or concentration of the antiseptic-disinfectant product and so, a higher toxicity. Thus, an efficient disinfection process should include a precleaning step to get rid of these organic materials. The old well-known principle of antisepsis-disinfection that only clean things can be efficiently disinfected is still valuable. Finally, in regard to the different studies on HCoVs' sensitivity to antiseptics-disinfectants, only few formulations are efficient within an adapted contact time and without a too-strong toxicity. For instance, considering their lack of efficiency against HCoVs, and also their toxicity, products only based on quaternary ammoniums or phenolic compounds should be avoided. Some largely used antiseptics-disinfectants such as ethanol or bleach show a significant activity on the HCoVs. However, some critical parameters should be considered, especially in the case of chlorine-derived compounds, such as the presence of organic materials that could prevent their antiseptic activity, or their dose-dependent effect on the HCoVs. The povidone-iodine or the chlorhexidine, when associated to ethanol and/or cetrimide, could be recommended when there is a risk of HCoVs contamination, contrary to another widely used antiseptic, the hexamidine."

Ebola virus

The highly infectious Ebola virus causes hemorrhagic fever in humans, and the virus is transmitted through direct contact with body fluids such as saliva, blood or feces from living or deceased patients with Ebola virus disease (EVD).

The Environmental Protection Agency (EPA) worked closely with the Centers for Disease Control and Prevention (CDC) to develop the *CDC Interim Guidance for Environmental Infection Control in Hospitals for Ebola Virus*. Although there are no EPA-registered products with specific label claims against the Ebola virus, enveloped viruses such as Ebola are susceptible to a broad range of hospital disinfectants used to disinfect hard, non-porous surfaces. In contrast, non-enveloped viruses are more resistant to disinfectants. As a precaution, the selection of a disinfectant product with a higher potency than what is normally required for an enveloped virus is being recommended by the CDC at this time. EPA-registered hospital disinfectants with label claims for hospital disinfection (or the equivalent microbial pathogen claims) and claims against non-enveloped viruses (e.g., norovirus, rotavirus, adenovirus, poliovirus) are broadly antiviral and capable of inactivating both enveloped and non-enveloped viruses and are used to disinfect environmental surfaces in rooms of patients with infectious diseases.

If a registrant has an EPA-registered product(s) that meets the criteria stated in the CDC guidance and the product was registered during or after 2010, or EPA has tested the product's efficacy under the Antimicrobial Testing Program, or the EPA has "confirmed" the product's efficacy, the registrant may identify such product(s) on company websites or through other non-label communications. Non-label communications should indicate that: the product meets the CDC criteria for disinfectant products with label claims for a non-enveloped virus; the product is intended for use on hard, non-porous surfaces; and the product's label use instructions for the non-enveloped virus or viruses should be followed. At this time, the EPA is not allowing label claims related to antimicrobial product efficacy specifically against the Ebola virus since a scientifically available testing procedure with a surrogate has not been developed.

The EPA provides a list of disinfectants for use against Ebola virus, available at: http://www.epa.gov/oppad001/list-l-ebola-virus.html. This list of registered disinfectants meets the CDC's criteria for use against the Ebola virus on hard, non-porous surfaces. It is necessary to follow the specific use instructions on the label for each disinfectant in order for the disinfectant to be effective. The product label will not specifically mention effectiveness against the Ebola virus. Instead, it will mention effectiveness against a different virus, such as norovirus, rotavirus, adenovirus, and/or poliovirus.

CDC's guidance recommends:

1. The use of an EPA-registered hospital disinfectant with a label claim for use against a non-enveloped virus (e.g., norovirus, rotavirus, adenovirus, poliovirus); and
2. The product label use directions for the non-enveloped virus or viruses should be followed when disinfecting against the Ebola virus.

In its *Interim Guidance for Environmental Infection Control in Hospitals for Ebola Virus*, the CDC notes, "The role of the environment in transmission has not been established. Limited laboratory studies under favorable conditions indicate that Ebola virus can remain viable on solid surfaces, with concentrations falling slowly over several days. In the only study to assess contamination of the patient care environment during an outbreak, Ebola virus was not detected in any of 33 samples collected from sites that were not visibly bloody. However, virus was detected on a blood-stained glove and bloody intravenous insertion site. There is no epidemiologic evidence of Ebola virus transmission via either the environment or fomites that could become contaminated during patient care (bed rails, door knobs, laundry). However, given the apparent low infectious dose, potential of high virus titers in the blood of ill patients, and disease severity, higher levels of precaution are warranted to reduce the potential risk posed by contaminated surfaces in the patient care environment."

As part of the care of patients under investigation (PUIs) or patients with confirmed EVD, hospitals are recommended to:

- Be sure environmental services staff wear recommended personal protective equipment (PPE) to protect against direct skin and mucous membrane exposure of cleaning chemicals, contamination, and splashes or spatters during environmental cleaning and disinfection activities. If reusable heavy-duty gloves are used for cleaning and disinfecting, they should be disinfected and kept in the room or anteroom. Be sure staff are instructed in the proper use of personal protective equipment including safe removal to prevent contaminating themselves or others in the process, and that contaminated equipment is disposed of appropriately.
- Use a U.S. Environmental Protection Agency (EPA)-registered hospital disinfectant with a label claim for a non-enveloped virus (norovirus, rotavirus, adenovirus, poliovirus) to disinfect environmental surfaces in rooms of PUIs or patients with confirmed EVD. Although there are no products with specific label claims against the Ebola virus, enveloped viruses such as Ebola are susceptible to a broad range of hospital disinfectants used to disinfect hard, non-porous surfaces. In contrast, non-enveloped viruses are more resistant to disinfectants. As a precaution, selection of a disinfectant product with a higher potency than what is normally required for an enveloped virus is being recommended at this time. EPA-registered hospital disinfectants with label claims against non-enveloped viruses (norovirus, rotavirus, adenovirus, poliovirus) are broadly antiviral and capable of inactivating both enveloped and non-enveloped viruses.
- Avoid contamination of reusable porous surfaces that cannot be made single use. Use only a mattress and pillow with plastic or other covering that fluids cannot get through. Do not place PUIs or patients with confirmed EVD in carpeted rooms. Remove all upholstered furniture and decorative curtains from patient rooms before use.

> "Limited laboratory studies under favorable conditions indicate that Ebola virus can remain viable on solid surfaces, with concentrations falling slowly over several days."
>
> **— CDC, 2014**

- Routine cleaning and disinfection of the PPE doffing area. Routine cleaning of the PPE doffing area should be performed at least once per day and after the doffing of grossly contaminated PPE. Cleaning should be performed by a healthcare worker wearing clean PPE. An EPA-registered hospital disinfectant with label claims against non-enveloped viruses (norovirus, rotavirus, adenovirus, poliovirus) should be used for disinfection. When cleaning and disinfection are complete, the healthcare worker should carefully doff PPE and perform hand hygiene.
- To reduce exposure among staff to potentially contaminated textiles (cloth products) while laundering, discard all linens, nonfluid-impermeable pillows or mattresses, and textile privacy curtains into the waste stream and disposed of appropriately.
- Ebola virus is a classified as a Category A infectious substance regulated by the U.S. Department of Transportation's (DOT) Hazardous Materials Regulations (HMR, 49 C.F.R., Parts 171-180). Any item transported offsite for disposal that is contaminated or suspected of being contaminated with a Category A infectious substance must be packaged and transported in accordance with the HMR. This includes medical equipment, sharps, linens, used healthcare products such as soiled absorbent pads or dressings, kidney-shaped emesis pans, portable toilets; and used PPE (gowns, masks, gloves, goggles, face shields, respirators, booties, etc.) or byproducts of cleaning contaminated or suspected of being contaminated with a Category A infectious substance.

Other Organisms

The pathogens of most concern to a healthcare institution may not necessarily be a more exotic organism; there are numerous epidemiologically important organisms, as Sydnor and Perl (2011) outline. These can include extended-spectrum beta-lactamase- and carbapenemase-producing Enterobacteriaceae. The most recently emerged carbapenemase is the New Delhi metallo-beta-lactamase (NDM-1). The NDM-1 gene is located on a plasmid and is easily transferrable to other organisms. These plasmids also often harbor genes conferring resistance to other classes of antibiotics. As Sydnor and Perl (2011) note, "NDM-1 has already been reported in other Enterobacteriaceae and non-Enterobacteriaceae Gram-negative organisms from around the world. The emergence of the NDM-1 strain is alarming given its rapid worldwide spread and the association with other genes conferring antimicrobial resistance, rendering strains carrying the NDM-1 gene resistant to almost all currently available antibiotics."

More routine organisms may be the culprit in infections far more often than MERS or Ebola, of course, and Weber, et al. (2010) remind us of the damage that garden-variety bugs such as methicillin-resistant Staphylococcus aureus and vancomycin-resistant Enterococcus spp., norovirus, Clostridium difficile, and Acinetobacter spp can cause. Of the latter three organisms, Weber, et al. (2010) note, "All three pathogens survive for prolonged periods of time in the environment, and infections have been associated with frequent surface contamination in hospital rooms and healthcare worker hands. In some cases, the extent of patient-to-patient transmission has been found to be directly proportional to the level of environmental contamination. Improved cleaning/disinfection of environmental surfaces and

hand hygiene have been shown to reduce the spread of all of these pathogens. Importantly, norovirus and C difficile are relatively resistant to the most common surface disinfectants and waterless alcohol-based antiseptics. Current hand hygiene guidelines and recommendations for surface cleaning/disinfection should be followed in managing outbreaks because of these emerging pathogens."

As Weber, et al. (2010) emphasize, "The CDC/Hospital Infection Control Practices Advisory Committee guidelines for environmental infection control in healthcare facilities and sterilization and disinfection in healthcare facilities should form the basis for institutional policies regarding surface disinfection. The scientific evidence has strongly suggested that contamination of surfaces in hospital rooms plays an important role in the transmission of MRSA and VRE. Recent evidence also strongly suggests that contaminated surfaces are important in the spread of the emerging healthcare-associated pathogens such as norovirus, C difficile, and MDR-Acinetobacter. For all three pathogens, as well as all MDR pathogens, enhanced cleaning and disinfection of all room surfaces are highly recommended when managing outbreaks. Studies have demonstrated that many room surfaces are not adequately cleaned, but that validated methods can be used to improve cleaning such as improved training of environmental service workers, use of checklists, and use of marker fluorescent dyes. Alternatively, the use of no touch disinfection methods such as ultraviolet light and vaporized hydrogen peroxide may be used. For norovirus and C difficile, the use of hypochlorite solutions (usually 1:10 diluted household bleach) has often been recommended for surface disinfection in hospital rooms as part of an intervention 'bundle' to control a healthcare-associated outbreak."

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