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# Outbreaks in Health Care Settings



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## KEYWORDS

• Outbreaks • Health care settings • Sources of outbreaks • Evaluation • Review

## KEY POINTS

- Outbreaks and pseudo-outbreaks that occur in health care settings should be approached systematically using advanced laboratory testing and epidemiologic tools to guide evaluation of events and to determine course of action.
- Multiple sources, such as health care personnel, the health care environment, supplies and equipment, and potable water, have been associated with outbreaks.
- Multiple organisms, such as atypical mycobacteria, *Acinetobacter*, *Pseudomonas*, *Staphylococcus aureus*, and carbapenem-resistant Enterobacteriaceae and fungal species have been associated with outbreaks in health care settings.
- Certain settings, including the neonatal intensive care unit, endoscopy, oncology, and transplant units, have specific issues that impact the approach to investigation and control of outbreaks in these settings.

## OUTBREAKS

Health care settings, while providing a safe environment for patient care, are complex settings and can produce conditions that facilitate the transmission of organisms and outbreaks. First, patients are vulnerable hosts due to immunosuppressive conditions, disruptions of their skin and mucous membranes, medications, and extremes of age. Second, the facility design, the multitude of life-saving invasive procedures using complicated equipment, contamination of the hospital environment with organisms (including multidrug-resistant organisms), the close proximity of patients who harbor transmissible organisms, and frequent contact with health care personnel, who can themselves transmit organisms, can provide an ideal environment for the propagation of an infectious agent.

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As more health care delivery has shifted from acute care hospitals to outpatient settings and the population ages and more individuals reside in nursing homes, outbreaks are increasingly recognized in alternative settings. The risk factors identified in acute care hospitals are also present in other locations. The entire continuum of health care needs to be considered in assessing the epidemiology of an outbreak.

Outbreaks can be expensive and time-consuming and can cause significant disruptions in health care operations in addition to impacting patient morbidity and mortality. Twelve percent of published outbreaks have led to closures of medical units. The most common pathogens associated with unit closure were not highly resistant organisms but rather, viruses such as influenza and norovirus.<sup>1</sup> Rotavirus and severe acute respiratory syndrome (SARS) were also associated with high closure rates.<sup>1</sup> The greatest challenges in outbreak management are the delay in identification of an outbreak and the delay in determining the source of the outbreak. In 37% of published outbreaks, the source is not identified. When the source is identified, it can be traced back to patients (25.7%), medical equipment or devices (11.9%), the environment (11.6%), and the staff (10.9%).<sup>2</sup> Interestingly, the most common pathogens identified in outbreaks are *Staphylococcus aureus* (14.8%), *Pseudomonas* spp (8.9%), and *Klebsiella* spp (7.1%), and these organisms are rarely associated with unit closures.<sup>2,3</sup>

## APPROACH TO AN OUTBREAK

An outbreak is defined as an increase in events, such as infections or number of organisms above the baseline rate, for a geographic area during a specified period of time. Some experts use a statistical definition. This increase may be a single infection, as in the cases of anthrax, health care-associated *Legionella*, or group A Streptococcal infection, or it may be many infections. The increase may occur over a short period of time or over years and may occur in a single unit or across many hospitals. Evaluating and managing outbreaks can be complex and multifaceted and often multiple steps occur concurrently. In any setting, the investigation should be efficient, thoughtful, and systematic so that appropriate infection prevention processes can be implemented to protect patients and health care personnel (**Box 1**).

Initially, it is important to verify the diagnosis. A varicella rash may be confused with smallpox or a culture may have been misread. Verification may require additional laboratory testing or clinical evaluation. It is, also, essential to communicate with the laboratory to save specimens early on in the investigation. These specimens can be used to identify a common source, trace transmission patterns, or reveal that a perceived outbreak was a cluster of unrelated events. Once the diagnosis has been confirmed, and the laboratory has been notified, a line list is created to describe potential cases with regard to person, place, and time. This is used to help focus the investigation. Simultaneously, it is important to determine if the baseline rate of the organism or infection of interest has changed over time, keeping in mind seasonal variation and comparing equivalent seasons. Such assessments must consider and ensure that other factors are not leading to the newly identified increase to accurately ascertain if there is a “true” increase in the rate of interest. A change in rates could result from altered surveillance definitions (changes in the numerator) or changes in the patient population sampled (changes in the denominator). As this assessment process is occurring, other cases should be identified, which may involve broadening the numbers and types of patients tested.

Once it has been determined that the observed infections represent an increase above baseline, the next step in investigating an outbreak is to create a case definition. This definition should be broad enough to capture any potential cases that may have

**Box 1****Outbreak investigation**

1. Verify the diagnosis and notify laboratory
2. Determine if this is an outbreak (baseline rates, assess changes in definition and changes in population)
3. Generate an epidemic curve and a line list (describe potential cases person, place, and time)
4. Perform a literature review to guide risk factor assessment
5. Develop a case definition
6. Find cases
7. "Shoe leather epidemiology" talk to staff, evaluate facility structure,
8. Implement appropriate infection-prevention interventions
9. Communicate with hospital leadership, and public relations department and risk department as indicated; involve public health authorities
10. Generate hypothesis and review cases for common epidemiologic links
11. Test the hypothesis (case-controlled evaluation)
12. Perform additional environmental or personnel screening as indicated
13. Evaluate impact of intervention

been missed on initial evaluation but not too broad to lose specificity in investigating any important epidemiologic links. Case finding should be performed systematically to avoid bias in data collection. Commonly this requires a review of the literature to understand incubation period, transmission dynamics, and common identified sources of a specific organism or syndrome (Table 1). Case definitions may need to be revised in the course of an investigation as new information becomes available. To identify cases, multiple data sources are available, including medical records, microbiology reports, operating room notes, respiratory therapy and procedure logs, or pharmacy records. Once case finding has been performed, generating an epidemic curve, which is a spatial presentation of the number of cases over time, aids in understanding transmission patterns. For example, these data may help differentiate a point source versus ongoing transmission and secondary transmission, and can help in assessing the phase of the epidemic.

These early steps are used to create and test a hypothesis by assessing if the suspected exposure differs in the cases from the uninfected patients (controls) to understand the relative contribution of risk factors to the outbreak. Depending on the situation (see Table 1), additional testing, such as environmental sampling from the patient's room or equipment, or testing of health care personnel and other patients to understand the extent of the outbreak may be undertaken. The epidemiologic review guides and supplements culture and clinical data in the investigative phase and is later used to evaluate the impact of the control measures implemented on the outbreak.

Importantly and in reality, measures to stop the outbreak are put into place before the hypothesis can be confirmed. In such situations, a line list of the cases with a list of possible exposures is used to simultaneously investigate epidemiologic links between cases and to implement control measures, such as changing a practice, enhancing a practice like hand hygiene, altering the number of personnel, enhancing isolation practices, testing personnel or patients, or closing a unit. These interventions should be

**Table 1**  
**Outbreak organisms**

Organism, Type of Infection(s) Associated with Outbreak, Process	Common Reservoirs	Potential Sources and/or Sites Associated with Outbreaks	Method of Detection: P = Patients, E = Environmental Source	Comments
<i>Acinetobacter</i> species Wounds, bloodstream and respiratory tract Infection and/or colonization	Wounds, genitourinary tract (GU), peri-rectal (PR) area, skin	Instrumentation, burns, trauma, surgery, respiratory equipment, gloves, parenteral nutrition, water	P = micro cultures E = surface swabs and culture of potentially implicated items	Intensive care units, patients returning from war zones; immunocompromised population Contaminates the environment extensively and can be difficult to eradicate
Adenovirus Epidemic keratoconjunctivitis (EKC); disseminated infection, cystitis	Oral pharyngeal secretions, urine	Equipment (tonometers) and health care workers	P = viral cultures, PCR E = not known to be useful	Ophthalmology patients, NICU patients, immunocompromised patients
<i>Aspergillus</i> spp Bloodstream, lower respiratory tract Infection and/or colonization	Air, dust, mold	Building demolition, renovation or construction sites, ventilation systems, dust-generating activities	P = microbiologic clinical (micro) cultures E = air sampling, surface samples	Often pathogenic in immunocompromised populations, and premature infants Can see increases with floods, severe weather events such as hurricanes
<i>Burkholderia cepacia</i> Bloodstream Infection and/or colonization	Oropharynx, skin	Water, contaminated solutions and skin disinfectants, contaminated equipment	P = micro cultures, stool E = cultures of potentially implicated items	Disinfectants (especially those containing iodine), water, solutions
<i>Candida</i> species Bloodstream	Skin (intertriginous areas)	Hands, onycholysis, devices	P = micro cultures E = cultures of hands and nail beds	Immunocompromised population at increased risk

<i>Campylobacter fetus</i>	Gastrointestinal	Food	P = micro cultures E = cultures of potentially implicated items/personnel	NICU patients at risk
<i>Enterobacter</i> species Urinary tract, bloodstream Infection and colonization	PR, bloodstream, wounds	Contaminated IV fluids, total parenteral nutrition Hands/dermatitis	P = micro cultures E = cultures of potentially implicated items	Intensive care units, reuse of calibrated pressure transducers
<i>Enterococcus faecalis</i> and <i>faecium</i> ( <i>Enterococcus</i> or Group D) Neonatal sepsis, cystitis, bacteremia Infection and/or colonization with resistant strains (VRE)	GU, PR, Gastrointestinal (GI) tract	Neonates/surgical patients/ transplant patients	P = stool, peri-rectal vaginal cultures; hand cultures E = used for vancomycin- resistant strains, primarily surface samples	Vancomycin resistant strains (VRE) do contaminate the environment and hands of health care personnel; environmental cultures are not used for susceptible strains
<i>Escherichia coli</i> Epidemic diarrhea, wounds and surgical incisions, urinary tract, bloodstream, neonatal sepsis or meningitis Infection	GI tract, skin, wounds	Equipment or fluids contaminated with organisms from lower GI tract, contaminated fluids	P = micro cultures, stool E = cultures of potentially implicated items	Very common normal flora
<i>E coli</i> O157:H7 and other hemorrhagic species Diarrhea and hemorrhagic colitis Infection	GI tract of animals	Contaminated water, and foods (meat, salads)	P = micro cultures E = cultures of potentially implicated items	Hemolytic uremic syndrome and thrombotic thrombocytopenic purpura are sequelae, high mortality among elderly and extremely young, cross contamination described
Hepatitis A Infection	Liver, stool, blood	Hands/foods, transfusion	P = micro cultures E = not known to be useful, cultures of potentially implicated personnel	Cross contamination described

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**Table 1**  
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<b>Organism, Type of Infection(s) Associated with Outbreak, Process</b>	<b>Common Reservoirs</b>	<b>Potential Sources and/or Sites Associated with Outbreaks</b>	<b>Method of Detection: P = Patients, E = Environmental Source</b>	<b>Comments</b>
Hepatitis B Infection	Liver, blood, and sterile body fluids	Blood and secretions, transfusions, improperly cleaned equipment, poor infection control practices	P = serology E = not known to be useful, cultures of potentially implicated personnel	Patients with diabetes, on dialysis, patients in psychiatric units
Hepatitis C Infection	Liver, blood, and sterile body fluids	Blood and secretions, transfusions, improperly cleaned equipment, multidose vials, poor infection-control practices	P = serology E = not known to be useful although recently integrated into an outbreak investigation, cultures of potentially implicated personnel	Patients on dialysis, patients in psychiatric units
Herpes virus infection Skin, pneumonia, mucosal surfaces Infection and/or colonization	Skin, saliva	Patients and health care workers	P = micro cultures E = not known to be useful	Outbreaks reported when patients shed or with lesions in health care workers
<i>Klebsiella pneumoniae</i> Urinary tract, pneumonia, bloodstream and neonatal infections Infection and/or colonization	PR, nares, mouth, wounds, skin, blood	Urinary catheters, hand lotions, contaminated fluids, ventilators, eczema Foodborne outbreaks recently reported	P = micro cultures E = cultures of potentially implicated items	Can be resistant to extended beta lactamases and carbapenemase; cross contamination described; rarely contaminates the environment
<i>Legionella pneumophila</i> and other species Pneumonia Infection	Water	Potable water, air conditioning units, cooling towers, ice machines, construction	P = micro cultures E = cultures of potentially implicated items/personnel	Can be associated with intense media scrutiny; 1 health care-associated case should trigger an investigation

<i>Listeria monocytogenes</i> Bloodstream and central nervous system infections Infection	Food	Contaminated foods	P = micro cultures E = cultures of potentially implicated items	Immunocompromised and mother-infant pairs at highest risk
<i>Mycobacterium tuberculosis</i> Respiratory Infection	Lungs, can disseminate	Airborne, improperly cleaned equipment	P = culture and PCR E = not known to be useful, cultures of potentially implicated personnel	Health care transmission suggests poor infection control
Nontuberculous mycobacteria ( <i>Mycobacterium avium</i> , <i>Mycobacterium goodnae</i> ) Respiratory, skin, bloodstream Infection and/or colonization	Lungs, skin	Contaminated water, improperly cleaned and sterilized equipment	P = micro cultures E = cultures of potentially implicated items	Associated with pseudo-outbreaks Reuse of improperly cleaned dialyzers, contaminated ice machines and other equipment
<i>Pseudomonas aeruginosa</i> Burns, wounds, urinary tract, pneumonia Infection and/or colonization	Gastrointestinal tract	Ventilators, whirlpools, sitz baths, solutions (mouthwash), any other water sources	P = micro cultures, stool, E = cultures of potentially implicated items	Primarily seen in immunocompromised patients and can be normal flora
<i>Ralstonia pickettii</i> Bloodstream	Skin, oropharynx, blood	Water including sterile, skin disinfectants, incubator water baths	P = micro cultures, stool E = cultures of potentially implicated items	Deliberate contamination of sterile fluids has been reported Neonates and immunocompromised hosts
<i>Salmonella</i> species GI infections, bloodstream Infection and/or colonization	GI and biliary tract	Contaminated food, dairy, eggs/poultry, contaminated blood products	P = stool, blood cultures E = not known to be useful	Not normal flora, cross contamination reported

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**Table 1**  
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Organism, Type of Infection(s) Associated with Outbreak, Process	Common Reservoirs	Potential Sources and/or Sites Associated with Outbreaks	Method of Detection: P = Patients, E = Environmental Source	Comments
<i>Serratia marcescens</i> Urinary tract, bloodstream, respiratory Infection and/or colonization	GI and GU	Solutions, inhalation therapy equipment, disinfectants, plasma, EDTA collection tubes, air conditioning vents, improperly cleaned equipment, chlorhexidine	P = micro cultures E = cultures of potentially implicated items	Cross contamination well described, reuse of calibrated pressure transducers
<i>Staphylococcus aureus</i> includes methicillin-resistant strains Surgical site, bloodstream Infection and or colonization	Human skin, anterior nares, skin, throat and upper respiratory tract, rarely rectal	Nasal/skin carriage in health care workers Increased nurse-to-patient ratios	P = microbiologic cultures E = hand and anterior nares cultures; rarely environmental cultures are indicated including settle plates if looking for a cloud spreader	Usually associated with surgical site and bloodstream infections, molecular and genotypic typing can determine whether there is a point source or technical problems. Point source can be from a carrier and would require cultures of staff and other patients; technical failures can lead to rhinovirus infection may be a risk factor, cross contamination well described for human shedding

<i>Staphylococcus</i> species (coagulase negative) Blood	Human skin	IV fluids, contaminated hands of health care workers, implanted devices	P = microbiologic cultures E = not known to be useful	Pathogenic in immunocompromised hosts and premature infants; commonly a contaminant
<i>Streptococcus pyogenes</i> (Group A) Deep wounds or intra- abdominal abscess, bloodstream infections	Upper respiratory tract, perianal area (rectum and vagina)	Carriage among health care workers	P = wound, stool cultures E = settle plates	Not commonly normal flora; threshold for a health care- associated investigation: 1 case
Varicella infections Skin, respiratory Disseminated or localized infection	Secretions and skin lesions	Poor ventilation	P = viral cultures, PCR or serology E = not known to be useful	Children and immunocompromised patients at risk Unvaccinated exposed can develop disease
<i>Yersinia enterocolitica</i> Bloodstream, GI tract	GI tract	Packed red blood cells	P = micro cultures E = cultures of potentially implicated items	—

Abbreviations: IV, intravenous; NICU, neonatal intensive care unit; PCR, polymerase chain reaction; PFGE, pulse field gel electrophoresis.

performed thoughtfully and through multidisciplinary groups representing all of the vested parties.

Communication is a critical part of an outbreak investigation. It is essential to keep hospital or entity leadership informed of findings and interventions in a timely and regular manner. It is helpful to include the legal team to advise on medico-legal issues. Communication outside the institution can be challenging and is best handled by an experienced individual who is credible, respected, and can speak to the issues and offer reassurance when appropriate. It also may be necessary and useful to communicate with the local health department depending on the specifics of the outbreak.

### **PSEUDO-OUTBREAKS**

Pseudo-outbreaks are defined as an increase in identified organisms but without evidence of infection. Sometimes, these can be difficult to distinguish from “true” clusters or outbreaks. Because pseudo-outbreaks generally represent contamination, identification of the source is important to prevent inappropriate treatment and additional testing in patients who do not have a true infection. Between 1965 and 2010, 72 clusters of pseudobacteremia have been published, 22 cases of pseudomeningitis, and 49 cases of pseudopneumonia. Pseudo-infections most commonly present as pseudobacteremias. Pseudobacteremias occur in the setting of contaminated culture media, contaminated antiseptics, contaminated blood culture vials, or inadequate disinfection of the analyzer. Although less common, pseudomeningitis has significant sequelae and has been due to contamination of procedure kits or culture media. Pseudopneumonia was most often due to mycobacterial species and was most often related to bronchoscopy.<sup>4</sup>

### **LABORATORY AND TESTING**

The expertise and collaboration of the laboratory is critical in the investigation of an outbreak.<sup>5</sup> As noted previously, it is essential to notify the microbiology laboratory of a potential outbreak and ask personnel to save any potentially related specimens. Laboratory testing plays an important role in outbreak investigation. The microbiology laboratory often identifies unusual organisms or clusters of the same organism and notifies the infection prevention department.

Microbiologic and molecular testing is continually evolving. In the past, determining relatedness of organisms was dependent on phenotypic methods. These methods include biotyping, which is the identification of genus and species or organisms, comparison of antibiotic susceptibility patterns, serotyping, and phage typing.<sup>6,7</sup> Serotyping involves the use of antibodies to bind antigens on the bacterial surface and phage typing assesses the sensitivity of the bacteria to various bacteriophage viruses.<sup>8,9</sup> Biotyping and antibiotic susceptibility testing are inexpensive and readily available in most clinical laboratories, but all of these phenotypic methods are limited in their sensitivity.

Over the past decade, many new genotypic approaches have become available and accessible and have allowed for greater resolution of specific strains. Plasmid typing was one of the first genotypic techniques used to type bacterial strains. Plasmids are extracted and a comparison of the number and types of plasmids is performed. The sensitivity of this technique can be enhanced by using restriction endonucleases. This method is time-consuming and is limited in its ability to discriminate strain relatedness in some organisms because plasmids can be mobile between species. Still this process may aid in the evaluation of a specific plasmid or transposon outbreak, which is suspected when different strains present with a similar resistance profiles.<sup>6,8-10</sup>

Pulse field gel electrophoresis (PFGE) has been considered the gold standard for molecular typing. Bacterial DNA is extracted and subsequently cleaved by specific restriction endonucleases, which are then separated in an agarose gel by a shifting electric field creating a pattern of bands known as restriction fragment length polymorphisms (RFLP), which can be used to compare strains.<sup>9,11</sup> A large proportion of the bacterial genome is assessed using this method, and there have been international fingerprinting databases that allow for standardized comparisons.<sup>7-9,11</sup> Ribotyping uses a similar process with more frequent cutting restriction endonucleases. After electrophoresis, the gel can be blotted onto a nitrocellulose or nylon membrane and a labeled DNA or RNA probe can be hybridized to the bacterial DNA. When rRNA is used as the probe, this technique is referred to as ribotyping.<sup>8,9</sup> Virtually all bacteria can be ribotyped, as this gene is highly conserved, but this process is less able to discriminate between strains than PFGE.<sup>8,9,12</sup>

DNA microarray hybridization is another way to type bacterial strains. In this process, DNA probes are attached to a surface and the DNA of the bacteria is isolated, labeled, and then hybridized with the DNA probes to be analyzed. This approach also allows for the detection of plasmids.<sup>11</sup>

More recently, polymerase chain reaction (PCR) techniques have been used to amplify certain DNA segments. Random amplification of polymorphic DNA (RAPD), also known as arbitrarily primed PCR (AP-PCR), uses primers that are specific to the bacterial strain, but not directed at specific sequences. This is a process that allows for multiple mismatches, so as to amplify DNA segments, which are then placed in agarose gel and electrophoresed. This process has been used frequently in outbreak investigations, as it is relatively easy to perform and fast, yet there is significant interlaboratory and intralaboratory variability with this technique.<sup>6,9,11</sup> Repetitive element PCR (rep-PCR) is similar to the RAPD process, but uses specific primers and more stringent amplification process. This process has been semiautomated in commercial machines.<sup>11</sup>

PCR can be used to amplify and sequence a specific gene as in the case of *emm* gene in group A streptococcus, or the protein A gene (*spa*) in *S aureus*. This process is referred to as single locus sequence typing (SLST).<sup>7,9,11</sup> In multilocus sequence typing (MLST), several specific housekeeping genes are amplified and sequenced. Each unique sequence is assigned a number and a sequence type (ST) is determined.<sup>7,9,11</sup> The most significant advantage of this method is standardization. It is, however, an expensive modality.

Optical mapping imbeds bacterial genomic DNA in agarose, which is then stretched in a microfluidic device. Restriction endonucleases are used to digest the bacterial DNA, which is stained with fluorescent dye and visualized by fluorescence microscopy. In this process, the individual genes remain in the order they are seen in vivo. A genomic optimal map can be created using specialized software. This technique is evolving, but its use is limited by cost and the need for specialized equipment.<sup>11</sup>

Whole genomic sequencing (WGS) is the newest tool in outbreak investigation in which the entire genome is sequenced.<sup>11</sup> This technique is becoming much more affordable, making it a viable option for outbreak investigation.<sup>7,11</sup> WGS has been used in outbreak investigations and has uncovered clusters of genetically related organisms that were unnoticed by phenotypic analysis alone,<sup>13</sup> has helped define previously unrecognized transmission patterns as in the case of *klebsiella pneumoniae* carbapenemase at the National Institutes of Health,<sup>14</sup> and has also shown that organisms, specifically *Clostridium difficile* and *S aureus*, thought to be related, were, in fact, genetically distinct.<sup>15,16</sup>

## SOURCES

### *Health Care Personnel*

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Health care personnel have been implicated in the transmission of gram-negative pathogens; respiratory pathogens, such as influenza, respiratory syncytial virus (RSV), pertussis, severe acute respiratory syndrome (SARS), and Middle East respiratory syndrome coronavirus (MERS-CoV); and gastrointestinal pathogens, such as *Salmonella* spp, Norovirus, and *C difficile*.<sup>17</sup> The most common source in these outbreaks is contact transmission, which is most often related to poor compliance with hand hygiene practices.<sup>2</sup> Artificial nails, rings, and dermatitis can reduce the effectiveness of appropriate hand hygiene practices and have been associated with outbreaks.<sup>18</sup> Rings and artificial nails are associated with higher rates of gram-negative carriage.<sup>18</sup> *Streptococcus pyogenes* has been associated with throat, rectal, and vaginal carriage and with outbreaks.<sup>19</sup> Health care personnel have been implicated as the primary source in fewer than 10% of *S pyogenes* nosocomial outbreaks, but 60% of health care personnel have been found to carry an outbreak strain.<sup>20</sup> *S aureus* has a predilection for the anterior nares and outbreaks have been associated with caregivers who are carriers.<sup>21</sup> This is discussed in more detail as follows.

### *Hospital Environment*

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The hospital environment has been increasingly linked to acquisition of organisms, especially *C difficile*, Norovirus, and multidrug-resistant organisms. Health care personnel frequently touch patients and room surfaces. In one study, 93 contact episodes were identified in 1 hour in medical, surgical, and neurosurgical units.<sup>22</sup> Contacts with the patient environment result in a 52% transfer rate of *S aureus*, vancomycin-resistant *Enterococcus* (VRE), and gram-negative bacilli, which is similar to the rate of transfer after touching patients.<sup>23</sup> These organisms persist in the environment and can persist on hands of health care personnel for several hours.<sup>24</sup>

It can be difficult to implicate environmental surfaces alone as a cause for transmission of infection, because of the uncertainty of the role of the many concurrent confounding variables. Nonetheless, most experts acknowledge the role of the environment in outbreaks. In a prospective cohort study in an intensive care unit, Hardy and colleagues<sup>25</sup> demonstrated that 11.5% of newly colonized patients become colonized with an environmental strain of methicillin-resistant *S aureus* (MRSA). Data from several studies show that colonization of a room from a prior occupant increases the risk that the new occupant will be colonized by 1.5-fold to 3.3-fold.<sup>23</sup> This association has been described with *Acinetobacter*, *C difficile*, *Pseudomonas*, VRE, and MRSA.<sup>23</sup> This risk can be mitigated through thorough cleaning, use of appropriate disinfectants, good compliance with cleaning protocols, and the use of no-touch technologies, such as hydrogen peroxide vapor.<sup>23</sup>

### *Waterborne Sources*

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Over the past century, better public water sanitation methods have reduced community-onset waterborne illness.<sup>26</sup> Nevertheless, outbreaks persist in hospital settings due to complex and antiquated water systems, and poor understanding of the risks to patients. Many organisms have been implicated in both pseudo and true waterborne outbreaks. Geography, weather, and infrastructure influence the types of organisms seen in waterborne outbreaks. The most commonly reported waterborne infection in North America is *Legionella*.<sup>27</sup> Between 2011 and 2012, the Centers for Disease Control and Prevention waterborne illness surveillance system identified drinking water as a cause of 66% of water-related outbreaks and in 26%

of these, the cause was *Legionella*. Other implicated organisms were Shiga-toxin producing *Escherichia coli*, *Shigella*, and *Pantoea agglomerans*.<sup>28</sup>

The transmission of waterborne pathogens to patients is likely related to build up of biofilm in plumbing structures, which are then dislodged into the water supply through increased use or construction. Patients may become exposed to the contaminants through showering, bathing, or drinking water or ice or through equipment that is rinsed in contaminated potable water. Not only is this contaminated water in direct contact with patients, but also with the environment and health care personnel, both of which can serve as fomites for transmission.<sup>29</sup>

*Legionella* infections garner significant media attention, yet they are relatively rare. In the United States, there were only 3000 cases in 2009 and 3500 cases in 2005 and 2006.<sup>30,31</sup> Furthermore, only 4% of these infections were associated with outbreaks.<sup>30</sup> *Legionella* presents as a nonspecific pneumonia and requires a specific antigen test for diagnosis and is therefore likely underdiagnosed as a cause of nosocomial pneumonia.<sup>32</sup> Although cooling towers and air conditioning units have been implicated as a common source for this organism, potable water, including hospital ice machines, account for most cases.<sup>33</sup>

### ***Legionella spp***

*Legionella spp* can be detected in 40% of freshwater samples by culture and in 90% by PCR.<sup>34</sup> It is particularly well adapted to cause infections in hospital settings. This organism thrives in water temperatures at 35°C and most organisms are found within biofilms rather than in free-flowing water, making it particularly difficult to disinfect plumbing and the associated contaminated biofilm.<sup>34</sup> A variety of disinfection methods have been used, including copper-silver ionization, chlorine dioxide, monochloramine, ultraviolet (UV) light, and hyperchlorination.<sup>35</sup>

Atypical mycobacteria have a predilection for water and frequently colonize potable water due to their ability to form biofilm. These organisms are difficult to culture, but modern techniques have demonstrated their importance in both outbreaks and pseudo-outbreaks, as discussed later in this article. Multiple species have been reported with *Mycobacteria mucogenicum*, *Mycobacterium gordonae*, *Mycobacterium simiae*, *Mycobacterium fortuitum*, and *Mycobacterium chelonae*.<sup>29,36</sup> These organisms have been shown to be responsible for both outbreaks and pseudo outbreaks, including in outpatient settings. Outbreaks have been traced to hospital water, dialysis water, fountains, ice machines, and hospital water supplies and disinfectant trays.<sup>37</sup>

Gram-negative organisms are emerging as important pathogens that can contaminate the water supply. Gram-negative organisms were reported in 79% of samples from 6 hospitals.<sup>38</sup> *Pseudomonas* from contaminated water in intensive care unit (ICU) settings have been linked by molecular testing to patient strains and to endoscope outbreaks.<sup>29,39,40</sup> In one of these outbreaks, Bukholm and colleagues<sup>39</sup> demonstrated that samples obtained from patients in an ICU were genetically identical (amplified fragment length polymorphisms) to water samples in the same ICU. Other organisms that have contaminated water-based supplies and equipment include *Pseudomonas spp*, *Ralstonia spp*, *Serratia spp*, *Aeromonas spp*, *Burkholderia spp*, *Acinetobacter spp*, and *Klebsiella spp*.<sup>29</sup> These organisms have been associated with outbreaks traced to contaminated ventilators, sitz baths, distilled water, pulsed lavage equipment, incubators, and hand creams.<sup>36</sup> Most recently and worrisome, Walsh and colleagues<sup>41</sup> described the contamination of the environmental water supply in India with the carbapenem-resistant New Delhi Metallobetalactamases (NDM-1) strains.

Other unusual organisms may be associated with waterborne outbreaks. One of the great controversies surrounds the importance of water as a source of fungi, such as *Aspergillus* spp., *Exophiala jeanselmei*, and *Fusarium* spp.<sup>29</sup> Norovirus also has rarely been linked to health care–associated outbreaks and traced to water sources.<sup>42</sup>

## ORGANISMS

### *Nontuberculous Mycobacteria*

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Nontuberculous mycobacteria (NTM) are ubiquitous in the environment in water and soil and can inhabit the health care environment.<sup>43</sup> Clinical infections peak in the late summer and early fall.<sup>44</sup> Health care–associated mycobacterial infections are almost exclusively due to rapid-growing NTM. These organisms have caused pseudo-outbreaks and outbreaks due to their predilection to contaminate water and are increasingly recognized as common causes of outbreaks. Most reported infections are related to surgical site infections and postinjection abscesses, as well as catheter-associated infections and cosmetic procedures.<sup>37</sup> Contamination of bronchoscopes and respiratory specimens are common causes of pseudo-outbreaks.<sup>43</sup>

The 2 most common surgeries associated with NTM infections have been cardiac surgeries and cosmetic surgeries.<sup>43</sup> An early cardiac surgery outbreak was attributed to infected porcine valves.<sup>43</sup> In subsequent cardiac surgery outbreaks it was difficult to identify a source until a postoutbreak analysis using more advanced laboratory methods typed mycobacterial species from previous outbreaks and found that in at least one outbreak, the mycobacteria isolated in the operating room could be traced to the water bath used in cardiac surgery and back to municipal tap water.<sup>43</sup> NTM outbreaks in cardiac surgery were significantly reduced after 1989, presumably due to the elimination of tap water and ice in the operating room.<sup>37</sup> A recent outbreak of *Mycobacterium chimaera* in cardiac surgery was traced a contaminated heater-cooler device that aerosolized the organism.<sup>45</sup>

In addition, other water-related mycobacterial outbreaks have been seen in hospital settings. Ice machines and hospital water have been the sources of outbreaks in susceptible patients.<sup>43</sup> Dialysis infections have also been caused by atypical mycobacteria.<sup>43</sup>

Augmentation mammography and other cosmetic surgeries are also a common procedure associated with rapid-growing NTM outbreaks.<sup>43</sup> The source has not been identified in most of these outbreaks, although the infections cluster around a particular plastic surgeon's practice suggesting a local environmental source.<sup>46</sup> Most (90%) of the sporadic cases were seen in Texas, North Carolina, and Florida.<sup>46,47</sup> In one particularly interesting case, 8 patients undergoing plastic surgery developed *M chelonae* infection attributed to dilution of gentian violet for marking with distilled water instead of alcohol.<sup>48</sup>

Atypical mycobacteria have been associated with mesotherapy and liposuction, including in medical tourists, and a surprising number of outbreaks have been related to tattoos.<sup>37</sup> There have been several outbreaks related to eye surgery,<sup>43</sup> including one recent outbreak implicating the humidifier in the room.<sup>49</sup>

### *Acinetobacter spp*

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*Acinetobacter* is one of the gram-negative organisms that is commonly seen in the setting of outbreaks. *Acinetobacter* genus consists of many different species and many of these species are found in soil and water, and in 40% of healthy humans, 17% of fresh fruits and vegetables, and in 21% of human body lice.<sup>50</sup> *Acinetobacter baumannii* is the most frequent cause of outbreaks and is rarely isolated from the

environment in nonoutbreak settings.<sup>50</sup> *Acinetobacter* resist desiccation and can survive for prolonged periods of time in hospital environments.<sup>50</sup> They also acquire resistance genes quickly, thus contributing to the importance of this species in nosocomial infections and outbreaks.<sup>51</sup> *Acinetobacter* has the largest known resistance island harboring 45 resistance genes acquired from *Pseudomonas*, *Salmonella*, and *Escherichia*, reflecting the species propensity to collect resistance genes.<sup>52</sup>

From 1977 to 2000, 51 outbreaks due to *Acinetobacter* spp. were reported, 29 (56%) involved respiratory infections and 22 (43%) were nonrespiratory sites, most commonly bloodstream and wound infection or simply colonization. In 26 (51%) of these outbreaks, a contaminated common source was found in respiratory equipment, humidifiers, and patient bedding.<sup>53</sup>

Because of its ability to survive in the environment, *Acinetobacter* frequently contaminates gowns and gloves used for isolation in health care settings.<sup>54</sup> Airborne dissemination of *Acinetobacter* has also been described.<sup>55</sup>

### ***Pseudomonas* spp**

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*Pseudomonas* is another gram-negative genus that is commonly a cause of health care-associated infections and outbreaks. Although *Pseudomonas* can cause infections in a variety of settings, it is commonly associated with immunocompromised hosts and ICU settings.<sup>56</sup> *Pseudomonas* spp infections can be difficult to treat due to the many antibiotic resistance mechanisms in this organism<sup>56</sup> and it can also develop resistance to biocides. Several outbreaks have been traced to contaminated benzalkonium chloride, povidone-iodine, and chlorhexidine.<sup>56,57</sup>

This organism can survive in hospital environments for extended periods of time and has been found in potable water, sinks, ultrasound gel, salads (up to 10<sup>3</sup> colony-forming units), skin creams, blood products, hemodialysis machines, and linens.<sup>58,59</sup> Outbreaks have been described in neonatal ICUs, hematology and oncology units, and other ICUs associated with a variety of sources and with various *Pseudomonas* spp.<sup>59</sup>

Health care personnel, family members, and visitors generally do not carry the organism, and transmission in health care settings is primarily linked to contaminated fomites, the environment, contaminated substances, or from patient-to-patient via contaminated hands.<sup>56</sup>

### ***Carbapenem-Resistant Enterobacteriaceae***

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Carbapenem resistance among gram-negative organisms is an important and emerging phenomenon and occurs by a variety of mechanisms, including chromosomal resistance (increase in amp C production), plasmid and mobile element-mediated resistance, and porin mutations.<sup>60</sup>

Importantly, resistance genes that are coded on plasmids are readily transmissible across species.<sup>60</sup> Using whole genomic sequencing, Conlan and colleagues<sup>61</sup> found horizontal transfer of carbapenem resistance among different species in the actual hospital environment.

Since carbapenemase resistance pattern was identified in 2001, other problematic strains such as NDM have emerged and the prevalence of carbapenem-resistant Enterobacteriaceae (CREs) in the United States has increased from 1.2% to 4.2%.<sup>62</sup> Interestingly this increase is largely fueled by clonal spread of a single clone of *Klebsiella* spp: ST258.<sup>60</sup> Infection with these organisms is challenging to treat and is independently associated with increased mortality.<sup>60</sup>

Many CRE outbreaks are associated with asymptomatic carriers and transmission from environmental sources, such as endoscopes and sinks.<sup>63</sup> Transmission is often silent and 50% of colonized patients are not detected through clinical cultures alone and



these asymptomatic carriers may be responsible for spread in health care settings.<sup>63</sup> Asymptomatic carriers are thought to be one of the mechanisms of spread in a 2012 NDM outbreak.<sup>64</sup> In another 18-person outbreak investigated using whole-genomic sequencing, complex and multiple modalities of transmission of CREs in the hospital were found and linked to asymptomatic carriers and environmental reservoirs.<sup>14</sup>

Various bundled interventions have been used to stop transmission in these acute outbreak settings, including increased compliance with hand hygiene, contact precautions, use of cohorting, enhanced environmental cleaning, active surveillance, and chlorhexidine bathing.<sup>65</sup>

### ***S aureus Including Methicillin-Resistant S aureus***

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*S aureus* is the second most common organism causing health care–associated infections<sup>66</sup> and the most common cause of published outbreak investigations.<sup>2</sup> Both methicillin-sensitive *S aureus* (MSSA) and MRSA carriage can be associated with deviations in practice, like poor hand hygiene compliance, overcrowding, and contact with human carriers.<sup>21</sup>

Approximately 33% of the US population is colonized with MSSA and 2% of the general population is colonized with MRSA, and colonization with either organism increases the risk of invasive infection (<http://www.cdc.gov/mrsa/tracking/index.html>).<sup>67</sup> Overall, 4.6% (0%–40%) of health care personnel carry MRSA.<sup>21</sup> The primary ecologic niche is the anterior nares, although the skin, and perineum also can be colonized.<sup>21</sup> Although poor infection control practices are risk factors for acquisition of *S aureus* among health care personnel, good infection control practices do not fully prevent health care personnel carriage and transmission.<sup>21</sup>

Most nasal carriers do not disperse *S aureus* or cause outbreaks, but nasal carriers can cause airborne dispersal in the presence of an upper respiratory infection or skin lesions, known as “cloud dispersal.”<sup>68</sup> Health care personnel are uncommonly the source of *S aureus* outbreaks. Among 191 MRSA outbreaks from 1966 to 2005, health care personnel were the source in 11 (5.8%), and in 8 (72%) of these, the implicated individual had either an upper respiratory infection, dermatitis, or skin infection.<sup>69</sup> In combined endemic and outbreak situations, 106 studies evaluated transmission from health care personnel to patients and found clear evidence of transmission in 27 (25.6%) studies and probable transmission in another 52 (49.1%) studies.<sup>21</sup> Due to the high prevalence of colonization in health care personnel, it is important to link epidemiologic findings with molecular typing to determine the source and appropriately decolonize the individual.<sup>21</sup> Because of the sensitivity and personal guilt associated with *S aureus* carriage and transmission to patients, the process requires extreme confidentiality and a thoughtful and caring approach.

The environment is also a potential source for MRSA outbreaks. Patient room environment is also colonized with MRSA in 73% of infected patient rooms and 65% of colonized patient rooms and can be a reservoir for outbreaks.<sup>70</sup> The higher the burden of *S aureus* in their nares, the more likely the person will shed organisms and have higher degrees of environmental contamination.<sup>71</sup>

### ***Fungus and Mold, Including Aspergillus***

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Mold infections cause significant morbidity and mortality in high-risk patients, especially those with impaired granulocyte dysfunction or immature or altered skin (ie, extreme prematurity or burns). Mold species are found throughout the health care environment and similar to other organisms, multiple studies have shown concordance between clinical isolates and environmental genotypes, highlighting the role of the environment in acquisition of these organisms.<sup>72</sup> *Aspergillus* spp outbreaks are the

best described of these organisms. *Aspergillus* has been associated with at least 60 outbreaks in health care settings.<sup>72-74</sup> Fifty percent of outbreaks have been attributed to construction, renovation, or demolition, and virtually all outbreaks are ultimately attributable to airborne dissemination from primary sources.<sup>74</sup> Fungal outbreaks have been associated with distribution of organisms through nearby construction, vacuum cleaning, contaminated carpet, contaminated air ducts, humidifiers, fireproofing material, rotting wood cabinets, and dressings, in-hospital plants, and tape.<sup>72</sup>

Installation of high-efficiency particle (HEPA) filtration has shown to be instrumental in prevention and abatement of fungal environmental contamination and clinical outbreaks.<sup>73</sup> However, sealing and repairing leaky or open windows, assessing water leaks in ceilings, maintaining appropriate air pressure relationships in patient care areas, and dust removal remain key strategies to prevent and abate fungal outbreaks occurring in the presence of HEPA filtration.<sup>72,74</sup>

Weather may play a significant role in fungal outbreaks. Several studies have documented seasonal variation of fungal spores with higher levels in the fall; however, these results are inconsistent and indoor samples do not correlate with outdoor samples.<sup>75,76</sup> The seasonal variation in the prevalence of *Aspergillus* spores inside a hospital has been associated with rainfall and internal relative humidity and temperature.<sup>76</sup>

Severe weather events such as floods and hurricanes have been associated with outbreaks of bacterial and fungal diseases. Most of these investigations have focused on bacterial pathogens.<sup>77</sup> Flooding in Thailand has been associated with fungal outbreaks and pseudo-outbreaks.<sup>77</sup> The 2005 tsunami in Sri Lanka resulted in an outbreak of *Aspergillus* meningitis due to contaminated supplies from poor post-flooding storage.<sup>78</sup>

### **Respiratory Infections**

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Respiratory infections are one of the most common types of infections encountered in the health care setting, and their importance and impact in this setting is being increasingly recognized. Most of these infections are transmitted by large droplets, but in some settings and situations, aerosolization is an important mode of transmission. Respiratory infections account for a large number of hospital admissions and hospital complications and can be a frequent reason to close a hospital unit, which disrupts hospital processes. Annual seasonal increases of respiratory infections during respiratory virus seasons can also lead to outbreaks within the health care setting. Viruses account for the largest proportion of identified pathogens (22%) in hospitalized patients with respiratory infections.<sup>79</sup> Of these, influenza A and B account for the largest proportion in patients older than 65 years and RSV is a significant pathogen in children and immunosuppressed patients.<sup>80</sup> Many outbreaks and sporadic cases have been attributed to influenza.<sup>81</sup> Attack rates in outbreak settings are as high as 55% among health care personnel and 37% of patients.<sup>82</sup> Health care personnel vaccinations are the mainstay of prevention for influenza and may reduce the incidence of nosocomial influenza.<sup>83</sup>

More recently, SARS and MERS coronaviruses have been reported in health care settings. Risk factors for transmission of these viruses include aerosol-generating procedures and failure to comply with recommended infection-control practices for contact and droplet precautions.<sup>84</sup> Both of these infections are associated with higher mortality rates and dramatic illness in health care providers and patients.<sup>84</sup>

Pertussis is a bacterial disease that has caused outbreaks in primarily pediatric health care settings.<sup>85</sup> There is significant morbidity and mortality in young unvaccinated infants.<sup>85</sup> These outbreaks can be difficult to manage due to the long latency period of pertussis, the infectiousness of the organism, and the activities and care

rendered in pediatric settings.<sup>85</sup> In one report, a single case cost \$75,000 to manage.<sup>86</sup> Pertussis cases have increased over the past 10 years,<sup>87</sup> and outbreaks are likely to increase due to the decreased immunogenicity of the acellular vaccine compared with the whole cell vaccine.<sup>88</sup>

Emerging respiratory viruses, like SARS and MERS coronavirus, and vaccine-preventable diseases, like pertussis and measles, continue to provide unique challenges in identification, diagnosis, control, and transmission.

### ***Gastrointestinal Infections***

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Gastroenteritis infections are common, and in settings in which rotavirus vaccine is available, norovirus is the leading cause of gastroenteritis epidemics across various health care settings and also in long-term care facilities, cruise ships, schools, and recreational activities. In a retrospective review of 90 outbreaks reported to health departments, 96% of nonbacterial gastroenteritis cases were ultimately attributed to norovirus.<sup>89</sup> Norovirus is a resilient, round virus that is spread through fecal oral contamination even before infected patients are symptomatic. It requires a low inoculum of virus to cause disease and can persist in the environment for days to weeks. Additionally, the virus has a high rate of genetic mutation, and host immunity is transient, making humans continually susceptible hosts. These factors lead to secondary attack rates of 30%.<sup>90</sup> Cleaning of environmental surfaces with hypochlorite can reduce the attack rate for norovirus.<sup>91</sup> Infection control interventions that work in this setting include restricting movement, screening staff and visitors and isolating those that are ill, enhanced cleaning and improved compliance, hand hygiene.<sup>91</sup>

*C difficile* is the most common pathogen identified in health care-associated infections in North America.<sup>66</sup> It is identified in the stool of 25% of hospitalized patients and in 2% to 3% of healthy adults.<sup>92</sup> To develop *C difficile* disease, 2 steps are needed: acquisition of the pathogen and alteration of gastrointestinal microbiome primarily through antibiotic use. Patients with active disease shed up to 100 million *C difficile* spores per gram of stool; hence, the organism has a predilection for the hospital environment and 20% to 51% of hospital room surfaces are contaminated in rooms of patients with active *C difficile* infection.<sup>93</sup> Hand of health care personnel are easily contaminated by spores after examining patients or even through contact of the patient's environment.<sup>94</sup> Daily cleaning reduces the risk of hand contamination.<sup>95</sup> Having a previous room occupant or roommate with diagnosed *C difficile* disease increased the risk the current occupant developing *C difficile* infection.<sup>23</sup> These data suggest an important role of the environment in the development of *C difficile* infection.

However, our understanding of *C difficile* epidemiology has evolved with the use of better laboratory tests, including whole genomic sequencing. Interestingly, despite the heavy and frequent environmental contamination with *C difficile*, only 25% of health care-acquired *C difficile* can be epidemiologically and genetically traced to another symptomatic contact, reemphasizing the importance of combined antimicrobial stewardship and infection-prevention strategies to prevent outbreaks.<sup>96</sup>

Gastroenteritis is extremely common in resource-limited settings, yet precious little is known about the pathogens in these settings. Organisms such as rotavirus, *Salmonella*, and enterotoxigenic *E coli* should be considered in these settings.<sup>97</sup>

## **HIGH-RISK SETTINGS**

### ***Neonatal Intensive Care Unit***

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The neonatal ICU (NICU) is unique environment with significant risks for outbreaks. Studies evaluating the unique physical environment in the NICU demonstrate the

importance of the facility design, and in fact, temporary facilities have been shown to have a higher rate of infection.<sup>98</sup> Modeling pathogen transmission in a NICU surrogate DNA demonstrated very rapid spread throughout the NICU.<sup>99</sup> In addition, neonates are particularly vulnerable to health care–associated infections. The prevalence of these infections is 5% to 24%; higher in premature infants than full-term infants.<sup>100</sup> Neonates have immature immune systems, require multiple invasive devices, and have multiple contacts with health care personnel.<sup>100</sup> For these reasons, NICUs account for 38% of ICU outbreaks and 18% of all published outbreaks.<sup>101</sup> The source of these outbreaks was identified in only 51% of outbreaks.<sup>101</sup> *Klebsiella*, *S aureus*, *Serratia* spp, and *Enterobacter* spp are the most common organisms identified. Patients were the source of 20% of outbreaks, contaminated equipment accounted for 12%, personnel were the source in 11%, and the environment contributed to 9%.<sup>101</sup>

Viral infections, including rotavirus (23%), RSV (17%), enterovirus (15%), and hepatitis A (11%) have been increasingly recognized as important pathogens among infants hospitalized in NICU settings.<sup>102</sup> Unsurprisingly, patients and personnel accounted for the source of transmission in 50% and 8% of viral outbreaks, respectively.<sup>101</sup>

*S aureus* and MRSA outbreaks are commonly reported in this unique setting.<sup>101</sup> Intravenous fluid may be a significant risk factor in this setting. Because of the common use of intravenous lipids, this is one of the settings in which *Malassezia furfur* is commonly seen.<sup>103</sup> Additionally, in resource-limited settings, bloodstream infection outbreaks with gram-negative organisms may be traced to poor sterile practices associated with mixing intravenous medications.<sup>104–106</sup>

Multiple interventions have been used to control outbreaks in this setting, most commonly reinforcing hand hygiene practices, active surveillance of patients, barrier precautions, and cohorting. Personnel screening was performed in 44% of outbreaks, most commonly associated with *S aureus* and modifications of care and equipment were implemented in 39% of NICU outbreaks.<sup>101</sup>

### **Endoscopes and Endoscopy Suites**

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As biomedical engineering in health care grows, more complex medical devices are being used to treat patients. These devices are increasingly recognized as sources of organisms that can be transmitted from patient to patient. Several studies have shown a high contamination rate, 1% to 2% to 50% to 60%, depending on sampling method in appropriately cleaned and disinfected endoscopes, highlighting the challenges with new technology.<sup>107</sup> The high rate of microbiological contamination may be in part due to the high prevalence of biofilms seen on endoscopes.<sup>108</sup>

Between 1966 and 2004, 19 reports of gastrointestinal endoscopy–related outbreaks were published. More than 90% of outbreaks linked to bronchoscopes and gastrointestinal endoscopes could have been prevented by better cleaning and disinfection processes.<sup>109</sup> Endoscopes have complex channels that make them difficult to clean properly.<sup>110</sup> *Pseudomonas* and multidrug-resistant *Klebsiella* spp and NTM have been associated with several outbreaks in which the cause was related to insufficient reprocessing.<sup>109</sup> A recent highly publicized outbreak of NDM-producing CRE resulted in 29 cases of colonization or infection in which no lapses in reprocessing were noted, suggesting that usual cleaning methods may not be effective in sterilizing complicated endoscopes with multiple moving pieces.<sup>111</sup> Similarly, an outbreak involving 32 cases of an AmpC-producing carbapenem-resistant *E coli* with 7 deaths was related to damaged endoscopes.<sup>112,113</sup>

Despite these reports and other challenges with determining how to safely reprocess endoscopes of all types, manual cleaning remains the cornerstone of practice

and can reduce the bioburden in colonoscopes up to 5 logs.<sup>110</sup> These recent outbreaks highlight the difficulties and cleaning and disinfecting new and important technologies with designs that do not lend themselves to the current processes.

### **Transplant Units**

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Infections are the leading cause of death in solid organ transplantation.<sup>114</sup> The first 30 days after transplantation are associated with procedure and health care–associated infections and are overwhelmingly due to bacterial infections.<sup>114</sup> Bloodstream infections are highest during the first month and then sharply decline after this period.<sup>115</sup> Multidrug-resistant organisms, particularly *Enterococcus* and gram-negative organisms, are frequent causes of infection in solid organ transplant patients.<sup>116</sup> Respiratory viruses, such as influenza, RSV, adenovirus, and rhinovirus, are common reasons for medical consultation and hospitalization in transplant patients. These viruses are more likely to cause lower lung involvement compared with healthy hosts, with relatively high mortality rates and can cause outbreaks in this patient population.<sup>117</sup>

Hematopoietic stem cell transplants are life-saving procedures for patients with leukemia and lymphoma. These procedures involve host bone marrow ablation, which results in profound immunosuppression until the autologous (host) or allogeneic (donor) bone marrow engrafts. Engraftment can take several weeks.<sup>118</sup> Gram-positive infections (20%–30%), gram-negative infections (5%–10%), *C difficile* (5%–10%), and respiratory viruses (15%) are the most common causes of infection in the preengraftment period.<sup>118</sup> The hospital environment poses significant risks to patients in this vulnerable time period. In addition, transmission from hands of health care personnel, and sources such as creams, mouthwash, sitz baths, and sinks, have been associated with infections in these patients.<sup>119</sup>

### **SUMMARY**

Outbreaks should be considered in any health care delivery site and can encompass a variety of pathogens and vectors of transmission. Epidemiologic and laboratory diagnostic tools can help guide a systematic investigation; however, often multiple steps occur simultaneously in the complex situations.

Many interventions have been used to abort an ongoing outbreak. Most significantly, it is important to ensure that basic infection prevention practices, such as hand hygiene and isolation, are in place and that health care personnel are compliant with these practices. Beyond this, prevention strategies need to be tailored to the epidemiologic findings, the organism, and the patients. The goal is to remove the offending source and protect patients and health care personnel.

Enhanced patient screening and surveillance are implemented 54% of the time, personnel screening in 38% of outbreaks, isolation or cohorting in 32%, enhanced or revised sterilization or disinfection practices in 24%, modification of care or equipment in 23%, increased use of protective clothing in 19%, and ward closure in 11%.<sup>2</sup> In most situations, these interventions are applied in combination and simultaneously, as there are limited data to empirically guide management.

Epidemiologic data are important tools in identifying potential sources and guiding additional testing. It is important to quickly implement reasonable prevention strategies, and communicate to leadership and public health authorities while refining further investigations. The goal is to abort further transmission or harm and provide a safe atmosphere for patient care while protecting the health care personnel and the institution. This harmonious balance requires engagement of all of the vested parties and access to necessary resources.

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