Hospital Infection Control: Considerations for the Management and Control of Drug-Resistant Organisms

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1 Introduction

The prevalence of hospital-acquired, antibiotic-resistant organisms has increased significantly over the last 20 years. Data from the National Healthcare Safety Network (NHSN) report published in 2013 revealed an alarming proportion of drug-resistant pathogens [1]. The NHSN system report represents data from more than 4000 medical facilities throughout the United States. Reports of hospital-acquired infections and microbiology data from participating institutions are published annually. From the sample, in 2009–2010, 43.7–58.7 % of all *S. aureus* isolates were resistant to methicillin, depending on the site of infection. *Enterococcus faecalis* and *Enterococcus faecium* were 6.2–9.8 % and 62.3–82.6 % vancomycin resistant, respectively [1]. An increase in drug-resistant staphylococci and enterococci has also been reported in Europe and South America [2–4].

As hospital-acquired infections with drug-resistant pathogens become increasingly more common and endemic, healthcare systems have taken various infection control measures to limit both their frequency and spread (Table 88.1, summary). Three parameters define the prevalence of drug-resistant bacteremia: how much enters the institution from outside, how much is selected by antibiotic use and misuse, and how much spreads from person to person [5]. The early recognition and isolation of incoming patients harboring resistant pathogens, appropriate antibiotic control programs, and assiduous infection control are necessary to minimize cross infection. Within the infection control domain, there may be specific efforts to minimize patient, healthcare worker (HCW), and environmental reservoirs and efforts to create meticulous hand hygiene and glove and gown use. In addition, surveillance systems for infection with hospital-acquired pathogens are essential for establishing endemic rates and for defining outbreaks. Aggressive surveillance for asymptomatic reservoirs may be of value but is not without controversy. Other considerations for an infection control program include hospital design considerations and antibiotic control programs.

1.1 The Importance of Patient and Healthcare Worker Colonization with Drug-Resistant Pathogens: Reservoirs for Infection

Colonization serves as a significant reservoir of drug-resistant, hospital-acquired pathogens. Patient colonization by drug-resistant pathogens such as VRE and MRSA has been well described. Thirty to 50 % of healthy adults have nasal colonization with *S. aureus*, with 10–20 % persistently colonized [6, 7]. Both methicillin-sensitive *S. aureus* (MSSA) and MRSA isolates can be persistent colonizers. Colonization with MRSA has been well documented in various healthcare settings. It has been reported that 25 % of patients admitted to a hospital will become nasally colonized with *S. aureus* [8]. This figure varies widely based on different populations and risk factors. Rates as high as 40–60 % have been reported in select populations including patients with diabetes and HIV. Certain populations are predisposed to colonization with *S. aureus* at the time of admission. Dupeyron et al. prospectively analyzed *S. aureus* colonization in a cohort of 551 cirrhotic patients. Screening nasal and rectal swabs were performed within 48 h of admission to the

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Table 88.1 Summary of selected infection control measures for the management and control of drug-resistant organisms

Infection control measure	Rationale	Comment
Nasal decontamination with mupirocin	• 25 % of patient admitted to a hospital will become nasally colonized with *S. aureus* • Compared with MSSA colonization, both MRSA colonization and MRSA acquisition during hospitalization increased the relative risk of infection	• In one prospective study, the use of intranasal mupirocin in a surgical cohort was effective in reducing the frequency of *S. aureus* hospital-acquired infections only in patients previously colonized with *S. aureus* • Mupirocin decreased the rate of *S. aureus* infections in hemodialysis patients
Chlorhexidine bathing	• Colonization of bacteria on patients' skin leads to environmental contamination • Environmental contamination increases the risk of transmission of hospital-acquired infections	• Chlorhexidine bathing decreases rates of colonization and hospital-acquired infections • Chlorhexidine-impregnated cloths provide a convenient no-rinse option • Studies revealed no significant toxicity associated with chlorhexidine bathing • Use is not approved for infants <2 months old
Environmental decontamination	• The inanimate environment can be contaminated with MRSA, *C. difficile*, VRE, and drug-resistant gram-negative rods. This is a potential reservoir for cross-transmission of hospital-acquired pathogens via the hands of HCWs	• All healthcare facilities should develop policies for the terminal and periodic disinfection of patient care areas and environmental services • This policy should include input from infection control practitioners, industrial hygienists, and environmental services supervisors • Ultraviolet light and hydrogen peroxide vapor are useful options for whole-room terminal cleaning
Hand hygiene	• Hand hygiene is the single most effective method to limit the spread of drug-resistant pathogens and hospital-acquired infections • Multiple opportunities exist in the hospital environment for the contamination of healthcare worker hands including direct patient care and contact with environmental surfaces	• Increased accessibility to hand hygiene agents is associated with improved compliance • Medicated hand washing agents are bactericidal (alcohol, chlorhexidine gluconate, triclosan) and effectively reduced bacterial counts on the hands • Chlorhexidine has the advantage of producing a residual antibacterial effect, thereby limiting hand recontamination until the time of the next hand hygiene episode • Sustained improvements in hand hygiene compliance should be achieved through a multimodal approach, which includes efforts that stress increased use of accessible, easy to use, medicated hand hygiene products, coupled with a hospital-wide, administration-backed, high-priority hand hygiene campaign • Novel hand hygiene technologies are emerging as useful methods for monitoring hand hygiene compliance
Gloves	• Gloves should be worn to prevent healthcare worker exposure to blood-borne pathogens and to prevent contamination of hands with drug-resistant pathogens during patient care activities	• Even with proper glove use, hands may become contaminated during the removal of the glove or with micro-tears that allow for microorganism transmission • Glove use should not be used as a substitute for hand hygiene
Gowns	• Several studies have documented colonization of healthcare worker apparel and instruments during patient care activities without the use of gowns	• The use of gloves *and* gowns is the convention for limiting the cross-transmission of hospital-acquired pathogens; however, the incremental benefit of gown use, in endemic settings, may be minimal
Healthcare worker apparel	• Contamination of healthcare worker apparel occurs throughout the course of a normal work day • Biological plausibility suggests that contaminated apparel could lead to transmission of organisms between patients	• Expert guidance by SHEA recommends implementing hospital-wide policies that include "bare below the elbows," restriction of white coats during patient care activities, and frequent laundering of apparel
Contact precautions	• Contact precautions are for selected patients who are known or suspected to harbor certain infections	• Contact precautions are commonly employed for the endemic control of MRSA, VRE. *C. difficile*, and multidrug-resistant gram-negative rods • Contact precautions are typically employed along with other infection control measures during hospital outbreaks of drug-resistant infections • Controversies in contact precautions include low compliance rates, increased rates of adverse events and anxiety/depression, and decreased satisfaction of care among patients on contact isolation

(continued)

Table 88.1 (continued)

Infection control measure	Rationale	Comment
Screening for asymptomatic patient colonization with drug-resistant pathogens	• Some authorities advocate active surveillance cultures to identify the reservoirs of MRSA and VRE • The goal of active surveillance is to identify every colonized patient so that infection control interventions such as contact isolation and cohorting can be implemented to reduce the risk of cross-transmission	• This measure is controversial • The majority of the studies had multiple interventions and major methodological weaknesses. As such, the quality of evidence in many studies was considered weak • The use of strict isolation practices may have a detrimental impact on the process and quality of patient care
Antibiotic control program	• Prolonged antibiotic prophylaxis with cephalosporins was an independent risk factor on logistic regression analysis for infections with cephalosporin-resistant gram-negative rods • Enteric VRE colonization has been associated with cephalosporin use • MRSA colonization has been associated with fluoroquinolone use	• The degree in which antibiotic pressure directly contributes to the cross-transmission of hospital-acquired infections remains poorly defined • All healthcare facilities are encouraged to implement multidisciplinary antibiotic stewardship teams, which should include a physician, pharmacist, clinical microbiologist, and infection preventionist

hospital. The investigators reported carriage rates of 19 % for MSSA and 16 % for MRSA. When comparing nasal carriers vs. non-carriers, the investigators documented a greater frequency of prior MRSA bacteremia and urinary tract infections, respectively, 8.3 % vs. 0.8 % and 11.4 % vs. 0.6 %. Additionally, the colonizing MRSA strain matched the invasive strain by pulsed-field gel electrophoresis [9].

In a different prospective series, however, only 2.7 % of the isolates were identified as MRSA [10]. Using a case control study and multivariate analysis to determine risk factors for MRSA colonization, independent predictors for colonization with MRSA were prior admission to a nursing home (OR 16.5) and a prior hospitalization of greater than 5-day duration within the past year [10].

Surveillance in nursing home settings reveals an increasing prevalence of *S. aureus* colonization. A prospective study in the mid-1980s by Sheckler et al. failed to document MRSA colonization in a cohort of community-based nursing homes [11]. Another study of community-based nursing homes from the early 1990s revealed 24 % of patients with *S. aureus* colonization, while 8.7 % of all patients were colonized with MRSA [12]. Lee et al. reported *S. aureus* colonization and infection in a 149-bed skilled nursing facility over a 1-year period. In this series, nasal and stool or rectal screening cultures were done on admission and then on a quarterly basis for a year. At the conclusion of the study, 35 % of all patients were colonized with *S. aureus* at least once during the period of analysis. Of the positive cultures, 72 % were MSSA, 25 % were MRSA, and 3 % were mixed phenotype. Only a minority of patients colonized developed an infection with *S. aureus*. The authors reported no association between MRSA colonization and frequency of *S. aureus* infection [13].

MRSA colonization has been studied in the intensive care setting. Garrouste-Orgeas et al. prospectively studied MRSA colonization and infection in a medical-surgical ICU of a tertiary care medical center [14]. In this prospective, observational study, cultures were obtained within 48 h of hospitalization, then weekly thereafter. Five percent of all patients were colonized with MRSA at the time of admission, and 4.9 % were newly colonized with MRSA during the course of their ICU stay. After multivariable analysis, factors associated with MRSA infection were severity of illness (HR 1.64), male gender (HR 2.2), and MRSA colonization (HR 3.84). However, MRSA colonization was not associated with increased mortality [14]. Overall, 10 % of patients in the cohort were colonized with MRSA. A similar rate of MRSA colonization has been documented by other investigators [15].

Co-colonization or coinfection with multidrug-resistant pathogens has been reported in several different populations. A point prevalence survey of antimicrobial-resistant pathogens in skilled care facility residents revealed a high rate of MRSA colonization. Of the 177 patients surveyed, 24 % were colonized with MRSA. Additionally, ESBL-producing organisms were discovered in their patient population, including *K. pneumoniae* (18 %), *E. coli* (15 %), and VRE (3.5 %). As these patients were asymptomatic, the investigators discovered a large, unrecognized pool of antimicrobial-resistant pathogens in their nursing home population [16]. Warren et al. determined the occurrence of co-colonization and coinfection with VRE and MRSA among medical patients in a medical ICU of a tertiary care medical center. Screening cultures were obtained in adults requiring at least 48 h of intensive care therapy. The study evaluated 878 consecutive patients. Of these, 40 % were either colonized or infected with VRE, 4.4 % were either colonized or infected with MRSA, and 9.5 % had either co-colonization or coinfection with MRSA and VRE. Risk factors for co-colonization or coinfection were increasing age, prior hospitalization within the preceding 6 months, and admission from a long-term care facility [17]. In a study of patients at high-risk

wards at an urban academic center, almost 30 % of patients carrying VRE were co-colonized with MRSA [18].

1.2 The Impact of Colonization Status on Hospital-Acquired Infections

An association between MRSA colonization and the subsequent development of MRSA hospital-acquired infections exists. Pujol et al. prospectively analyzed the relationship of MRSA nasal colonization and bacteremia [19]. During a 1-year period in an ICU, nasal swabs were obtained on all patients within 48 h post admission and then weekly. Thirty percent of all patients were nasal *S. aureus* carriers: 17 % with MSSA and 13 % with MRSA. Bacteremia was observed in 38 % of the MRSA carriers and 9.5 % of the MSSA carriers. Using Cox proportional hazard modeling, the relative risk (RR) of *S. aureus* bacteremia was 3.9 when comparing MRSA to MSSA nasal carriers [19].

Other investigators have confirmed the significance of MRSA colonization and its predilection for subsequent infection. Davis et al. investigated MRSA colonization at hospital admission and its subsequent effect on MRSA infection rates [20]. Nares cultures were obtained on admission on patients admitted to various hospital units, including medical, surgical, and trauma ICUs. The patients were followed for the study period and then 1 year thereafter. Nasal colonization with MSSA far exceeded that with MRSA (21 % vs.3.4 %). However, 19 % of patients with MRSA colonization at admission and 25 % with subsequent colonization developed infection with MRSA. Reported infections included line sepsis, bacteremia, and skin and soft tissue infections. Compared with MSSA colonization, both MRSA colonization and MRSA acquisition during hospitalization increased the relative risk of infection (RR 13 and RR 12) [20].

Nasal carriage of both MRSA and MSSA has been associated with increased risk of vascular access-related infections in patients with type II diabetes on dialysis. In this series, nasal swabs were performed in 208 patients enrolled for long-term hemodialysis between 1996 and 1999 [21]. Persistent nasal carriage was defined as two or more positive cultures. Diabetic patients had higher MSSA and MRSA carriage rates (54 and 19 %) than nondiabetics (6 %). Overall, 73 % of all diabetic patients were colonized nasally with either MRSA or MSSA. Additionally, when compared to nondiabetic hemodialysis patients, the relative risk for vascular access-associated bloodstream infection was significantly greater [21].

Lastly, published data suggest that healthcare workers colonized with drug-resistant pathogens may be associated with cross-transmission and hospital-acquired infections. Wang et al. investigated a hospital-acquired outbreak of MRSA infection initiated in a surgeon carrier [22]. Over a 4-month period, five patients who had undergone open-heart surgery developed surgical wound infections and mediastinitis with MRSA. Investigation by the infection control team led to MRSA nasal screening of all ICU staff and of the surgical team. Pulsed-field gel electrophoresis technology was employed for isolate typing. Of the five hospital-acquired MRSA infections, all had the same attending surgeon and 2–3 assistant surgeons. Surveillance cultures of the staff were all negative save for one assistant surgeon, present in all of the five cases. The typing profile of the surgeon's isolate was identical to that of three of the cases. The remaining two isolates were lost and hence not typed; however, these were presumed to be identical to the others owing to the same antibiogram [22]. Other investigators have reported healthcare colonization and its effect on cross-transmission and subsequent MRSA infection and colonization. Boyce et al. reported the spread of MRSA within a hospital. A healthcare worker with chronic sinusitis was the purported source [23]. In addition, outbreaks of MRSA infections in a burn unit have implicated nursing staff as sources [24, 25].

1.3 Strategies for Staphylococcal Decolonization

Given the importance of *S. aureus* as a hospital-acquired pathogen, decolonization of carriers has been attempted in various populations. Early investigations employed both topical and systemic therapy for the eradication of *S. aureus* nasal colonization. In the 1980s, in experimental studies, it was shown that mupirocin was effective in reducing nasal carriage of volunteers with methicillin-sensitive *S. aureus* [26]. Subsequently it was shown that mupirocin was active against methicillin-resistant strains of *S. aureus* [26]. In the early 1990s, Darouich et al., as part of a multidisciplinary approach, attempted to control the spread of MRSA within a spinal cord unit [27]. Eleven patients in the spinal cord unit were colonized with MRSA. The sites of colonization varied but included nares, axilla, tracheostomy site, urethra, wounds, and urine. Ten of the colonized patients received a 2-week course of 100 mg of minocycline twice daily and 600 mg of rifampin once daily. The remaining patient was treated for only 1 week with the minocycline/rifampin combination. For those that were nasally colonized, nasal mupirocin ointment was applied twice daily for 5 days. The authors reported eradication of MRSA colonization in 10 of the 11 patients [27].

Subsequent data suggest that for nasal MRSA, mupirocin alone may be sufficient for decolonization. In one, 6-month, two-step, prospective study from France, the efficacy of nasal mupirocin for the prevention of *S. aureus* nasal carriage was assessed [28]. In the first 4 months, all patients in the surgical ICU were cultured without the nasal decontamina-

tion protocol. Nasal and surgical wound swabs and tracheal secretions were collected on admission and then once weekly. In the following 2 months, all patients admitted to the SICU were given twice daily intranasal mupirocin for 1 week. In the comparison, 31.3 % of untreated patients and 5.1 % of mupirocin-treated patients subsequently acquired nasal *S. aureus* while in the surgical ICU. In addition, nasal carriers were more commonly colonized in the bronchopulmonary tract and surgical wounds (62 %) than were nonnasal carriers (14 %). When compared to the nontreatment group, the bronchopulmonary tract infection rate was reduced in the group receiving mupirocin treatment. Thus, in a surgical ICU cohort, the use of prophylactic mupirocin treatment reduced the rate of both MRSA nasal colonization and subsequent MRSA colonization bronchopulmonary infection [28]. Additionally, the use of mupirocin has successfully decreased the rates of *S. aureus* infections in dialysis patients, even though most of these isolates were methicillin sensitive [29].

Intranasal mupirocin has been employed to prevent postoperative *S. aureus* infections. Perl et al. conducted a randomized, double-blind, placebo-controlled study to determine the efficacy of mupirocin in both the reduction of surgical site infections and in the prevention of other hospital-acquired infections [30]. A total of 3864 patients were included in an intention to treat analysis, and of these, 891 patients (32.1 %) were *S. aureus* colonized in the anterior nares. The cohort underwent either general, gynecologic, neurologic, or cardiothoracic surgery. At the conclusion of the study, 2.3 % of the mupirocin recipients and 2.4 % of the placebo recipients had *S. aureus* infections at the surgical site. However, in a subset analysis of *S. aureus* nasal carriers who received mupirocin, there was a statistically significant reduction in the rate of *S. aureus* hospital-acquired infections, 4.0 % versus 7.7 % for recipients of placebo. Thus, in this analysis, the use of intranasal mupirocin in a surgical cohort was effective in reducing the frequency of *S. aureus* hospital-acquired infections only in patients previously colonized with *S. aureus*. For patients known to be nasal carriers of *S. aureus*, consideration should be given to the preoperative application of mupirocin.

The above studies used a targeted approach to decolonization of patients colonized with MRSA, which requires active detection and isolation of the organism. This approach can be costly, both directly and indirectly [32]. Universal decolonization, which involves the broad use of infection prevention practices throughout populations that are at high risk of hospital-acquired infections, is favored by some as a preferred approach[31]. Huang et al. conducted a pragmatic, cluster-randomized trial to assess which approach is superior [32]. The study randomized 74,256 patients from 43 hospitals into three groups. The group that underwent universal decolonization had significantly lower rates of MRSA-positive clinical isolates when compared to either screening and isolation or targeted decolonization groups. Universal decolonization also resulted in decreased rate of bloodstream infections due to any pathogens. There was no significant difference in the number of MRSA bloodstream infections between the groups.

1.4 The Role of Chlorhexidine (CHG) Bathing for Prevention of Hospital-Acquired Infections

Chlorhexidine is an antiseptic that has activity against a broad spectrum of organisms, including gram-negative bacteria, gram-positive bacteria, and fungi [33]. Chlorhexidine bathing has been employed as a means to decrease bacterial burden on patient skin. Bathing or showering with a 4 % solution is effective in reducing bacterial density on the skin of patients [34, 35]. Recently, cloths impregnated with 2 % CHG have become widely available as a no-rinse option as well. One study demonstrated that 2 % CHG cloths may perform superiorly to topical application of 4 % CHG [35]. Chlorhexidine-impregnated cloths have also demonstrated effectiveness in reducing bacterial burden of multidrug-resistant organisms like *K. pneumonia* and MDR GNR on skin surfaces [36]. In 2012, Karki and Cheng published a systematic review that assessed the impact of CHG bathing (with CHG-impregnated cloths) on the incidence of healthcare-associated infections and colonization. The authors included 20 studies in the analysis: 15 quasi-experimental studies, 3 cohort studies, 1 crossover study, and 1 randomized controlled study. The final analysis demonstrated reduced rates of MRSA and VRE colonization and reduced rates of hospital-acquired infections with CHG bathing. There were no reports of significant toxicity for patients who underwent daily CHG bathing [37]. Subsequently, a multicenter, cluster-randomized, nonblinded crossover trial also concluded that CHG bathing reduces rates of colonization and CLABSI. The overall rate of acquisition of multidrug-resistant organisms was lower with the use of CHG-impregnated cloths than with the use of nonantimicrobial washcloths (5.10 cases per 1000 patient days versus 6.60 cases per 1000 patient days, respectively). This same study demonstrated significantly reduced rates of hospital-acquired bloodstream infections with the use of CHG-impregnated washcloths versus nonantimicrobial cloths (4.78 cases vs. 6.60 cases per 1000 patient days, respectively). Interestingly, central line-associated fungal bloodstream infections were also reduced with CHG bathing [38].

Two studies support the use of CHG bathing in children as well. One quasi-experimental study that included adult and pediatric patients found a significant reduction in *Clostridium difficile* infections with the use of CHG bathing. Compared to the baseline period when no CHG bathing was done, all cohorts that used CHG bathing had a lower relative risk of *C.*

difficile infection [39]. A multisite, cluster-randomized, crossover trial which was conducted in ten pediatric ICUs and involved 4947 patients demonstrated a reduction in the rate of bacteremia in patients receiving daily CHG bathing compared to those receiving standard bathing practices. Although reduction in the rate of bacteremia using intent to treat analysis was not statistically significant, the per protocol analysis did reveal a significant reduction in the rate of bacteremia. No serious adverse events were reported. However, more patients in the intervention group reported skin irritation [40]. Of note, these studies assessed tolerability and effectiveness of CHG in children greater than 2 months of age. Chlorhexidine is not currently approved by the US Food and Drug Agency for use in children less than 2 months of age due to the possibility of irritation or chemical burns [41].

Some concern for development of bacterial resistance to CHG and selection of resistant organisms with the use of CHG exists. There is a paucity of data on this topic, but reduced in vitro susceptibility to CHG have been reported [42, 43]. One study demonstrated higher MICs to CHG among a multidrug-resistant strain of *K. pneumonia*. Of the multidrug-resistant *K. pneumonia* isolates, 99 % had MICs >32 μg/mL, compared with 52 % of other *K. pneumonia* strains [42].

1.5 Environmental Contamination

It is well documented that patients colonized or infected with drug-resistant pathogens, such as MRSA, VRE, or multidrug-resistant gram-negative rods, contaminate the inanimate environment. Contaminated objects can include but are not limited to floor, bed linens, patient gowns, overbed tables, bedrails, urinary containers, enteral feeding tubes, light switches, bathroom faucets, IV pumps, telephones, and blood pressure cuffs [23, 44–46]. In addition to objects in patient rooms, contamination can extend beyond the immediate patient care area. Devine et al. surveyed two acute care hospitals (A and B) in the United Kingdom with a focus on contamination of ward-based computer modules [47]. In total, 24 % of sampled computer terminals were positive for MRSA. Five of the six positive computer terminal cultures were from hospital A. In contrast to hospital A, the infection control team of hospital B reviewed handwashing compliance regularly with doctors and nurses. Hospital B also reported a greater rate of paper towel consumption, a surrogate marker for hand hygiene compliance. Although the direction of transfer is impossible to define from such studies, the data suggest that inanimate reservoirs have the potential to contaminate the hands of healthcare workers. Furthermore, hand hygiene compliance may be essential in minimizing this risk of environmental contamination [47]. Contamination of gowns and gloves from hospital personnel (those performing nursing care activities on colonized patients and those with no direct patient contact) has also been documented [23].

The environment likely represents a potential source for healthcare worker hand contamination, an important step in the cross-transmission of hospital-acquired pathogens. A study by Duckro et al. gave credence to this idea [48]. Cultures were obtained from the intact skin of 22 patients colonized with VRE and from various environmental sites before and after routine care by 98 healthcare workers. Cultures were obtained from the hands of the HCWs before and after patient care, and pulsed-field gel electrophoresis typing of the isolates was performed. In this analysis, VRE was transferred from contaminated sites in the environment or on the patient's intact skin to clean, previously non-contaminated environmental and body sites via the HCW in 10.6 % of the opportunities. Of these 16 VRE transfer sites, 12 were patient body sites [48]. These data suggest that the hospital environment is a potentially important reservoir for cross-transmission of drug-resistant pathogens.

As patients colonized with resistant pathogens can contaminate the environment, proper environmental disinfection is an important step for minimizing the risk or cross-transmission. An extensive review of approved disinfectants and environmental cleaning practices is beyond the scope of this chapter. However, several general principles are of note. Terminal cleaning of patient rooms should aim to minimize the persistence of drug-resistant pathogens. Hospital environmental services personnel should clean the bed frame and handrails, mattress, and all other patient room furnitures with an Environmental Protection Agency (EPA)-approved disinfectant and use according to manufacturers' guidelines [49]. Suction containers should be removed and prepared for disposal or reprocessing, and all other reusable equipment should be decontaminated using an (EPA)-approved disinfectant. The bathroom in an isolation room should be thoroughly cleaned and disinfected, with particular attention paid to the sink, toilet, and doorhandle areas. Environmental surfaces with a high degree of patient body and hand contact such as bedrails, doorknobs, bathrooms, light switches, and wall areas should be cleaned with greater frequency and not exclusively at the time of patient discharge.

Traditional room decontamination may not be sufficient to eliminate environmental bioburden. Therefore, alternate methods for terminal disinfection of patient rooms are needed. Ultraviolet (UV) light irradiation has the ability to inactivate a wide range of biological agents. Rastogi et al. studied the effectiveness of UVC light for decontamination of three hospital surfaces (aluminum bed railings, stainless steel operating tables, and laboratory coats) [50]. *Acinetobacter baumannii* was inoculated onto small coupons of each of the three types of materials. Fifteen minutes of

UVC light exposure (at a fluence of 90 J/m [2]) resulted in ≥4-log reduction and complete killing of organisms on the two metal surfaces. However, UVC light was ineffective for laboratory coat disinfection [50]. In addition to inadequate penetration of fabrics, the use of UV light for whole-room disinfection has the disadvantage of providing only "line-of-site" killing.

Like UV irradiation, hydrogen peroxide vapor (HPV) inactivates a wide range of biological agents through production of oxygen free radicals. Its effectiveness was demonstrated in one prospective cohort intervention study [51]. The intervention (HPV) was implemented after routine cleaning and disinfection of rooms with a quaternary ammonium compound. All rooms were previously occupied by patients with known infection or colonization with multidrug-resistant organisms. Patients admitted to rooms that underwent HPV decontamination were 64 % less likely to acquire any multidrug-resistant organisms than those that were in rooms with no HPV decontamination. Specifically, patients in rooms with HPV decontamination were 80 % less likely to acquire VRE [51].

Several potential strategies exist for monitoring compliance and assessing environmental hygiene. Boyce et al. compared three methods of monitoring with a prospective observational study of 100 hospital rooms [52]. In this study, five high-touch surfaces were marked with different brands of fluorescent markers prior to terminal cleaning and were checked after cleaning with a black light to assess whether the marker had been partially or entirely removed. Aerobic colony counts (ACCs) and adenosine triphosphate (ATP) bioluminescence assays were performed on the same surface before and after terminal cleaning. The ATP method was much less likely than either fluorescent markers or ACC to classify a room as clean. This result is not surprising since ACC measures only contamination by aerobic bacteria, whereas ATP bioluminescence assays detect many ATP-containing organic substances such as secretions, blood, and food. The authors concluded that each method has utility for different situations. Fluorescent markers are simple to implement and are useful for providing feedback to housekeepers regarding adequacy of cleaning. Aerobic colony counts provide a quantitative measurement of surface contamination and provide information about specific organisms causing contamination, but are costly and time consuming. Advantages of ATP bioluminescence assays are ease of use, rapid results, and provision of quantitative measurements that can be used for trends and feedback [52].

All healthcare facilities should develop policies for the terminal and periodic disinfection of patient care areas and environmental services. This policy should include input from infection control practitioners, industrial hygienists, and environmental services supervisors.

2 Hand Hygiene

Hand hygiene, either by conventional handwashing or disinfection, is the single most effective method to limit the spread of drug-resistant pathogens and hospital-acquired infections [53]. Conceptually, the cross-transmission of hospital-acquired pathogens is summarized as follows [54]:

- Organisms present either on the patient's skin or from the inanimate environment must be transferred to the hands of the healthcare worker.
- Hospital-acquired pathogens must be capable of surviving on the hands of the healthcare worker.
- Hand hygiene must be either inadequate or omitted.
- The contaminated hands of the healthcare worker must then come into contact with another patient or into contact with an inanimate surface that will later come into contact with the patient.

The microorganisms of the hand can be divided into transient flora and resident flora [55]. The resident flora is typically of low virulence pathogens such as *Micrococcus*, coagulase-negative *Staphylococcus*, and *Corynebacterium*. These organisms are difficult to remove by handwashing yet are rarely pathogenic except when introduced to the patient by invasive procedures. Transient flora is acquired largely by contact with either the patient or an inanimate object, is loosely attached to the skin, and is easily removed by handwashing [55]. These organisms include MRSA, VRE, and MDR GNR. Additionally, these bacteria are important causes of hospital-acquired infections.

Numerous studies have shown that multiple opportunities exist in the hospital environment for the contamination of healthcare worker hands. Hospital-acquired pathogens can be recovered from a variety of patient care scenarios. Patient contact, including contact with wounds and intact skin, can result in healthcare worker hand contamination [56–67]. Areas of high hospital-acquired pathogen concentration on patient skin include the axillae, trunk, perineum, inguinal region, and hands [59, 61, 62, 64, 66–68]. As previously mentioned, the inanimate environment is a source of contamination.

Healthcare workers should practice hand hygiene before and after each patient contact. Methods of hand hygiene include washing with plain soap and water, or using an antibacterial agent such as alcohol, chlorhexidine gluconate, or triclosan as either detergent washes or waterless hand-rubs. Conventional soap and water may have various shortcomings and barriers to compliance. Although soap and water can remove loosely adherent transient skin, these agents have minimal antimicrobial activity [54]. For effective bacterial reduction, a 30 s hand rub is recommended; unfortunately, this time length of handwashing is rarely practiced. In

addition, several studies have demonstrated that handwashing with both plain soap and water can result in skin irritation, dryness, and a paradoxical increase in microbial counts on the skin [69–73]. Medicated handwashing agents are bactericidal (alcohol, chlorhexidine gluconate, triclosan) and effectively reduce bacterial counts on the hands. Moreover, chlorhexidine has the advantage of producing a residual antibacterial effect, thereby limiting hand recontamination until the time of the next hand hygiene episode [74].

At least one study supports the effectiveness of chlorhexidine as a hand antiseptic agent with regard to infection control endpoints. Doebbling et al. compared different hand hygiene agents with the end result of hand hygiene compliance observation and the reduction of hospital-acquired infections in an intensive care unit setting [75]. During an 8-month period, a prospective, multiple crossover trial was conducted in three intensive care units. The trial involved 1894 adult patients exposed to alternate months of either chlorhexidine or 60 % alcohol solution with the optional use of a non-medicated soap. A greater frequency of hospital-acquired infections was seen with the combination of alcohol and soap compared to the chlorhexidine hand hygiene agent (202 vs. 152). However, during periods of chlorhexidine use, there was a decrease in the rate of hospital-acquired infections and an increase in the observed frequency of hand hygiene compliance coupled with a volume of chlorhexidine consumption that exceeded that of the alcohol-based agent. The difference in hospital-acquired infections may have been partly due to increased compliance with hand hygiene practices. Regardless, owing to their bactericidal properties, medicated hand hygiene agents, including chlorhexidine, alcohol, and triclosan, should be highly considered especially in environments with elevated rates of drug-resistant pathogens.

Unfortunately, data on healthcare worker hand hygiene practice are discouraging. The reasons for poor compliance are multiple and have been studied by numerous investigators. Observational studies of hand hygiene compliance report compliance rates of 5–81 % [76–108]. Factors cited that may influence poor adherence with hand hygiene include insufficient time, understaffing, patient overcrowding, lack of knowledge of hand hygiene guidelines, skepticism about handwashing efficacy, inconvenient location of sinks and hand disinfectants, and lack of hand hygiene promotion by the institution [54].

In the intensive care units, where critically ill patients are particularly susceptible to hospital-acquired infections, hand hygiene is poor. A British study performed a detailed survey of hand hygiene practices in 16 ICUs [55]. Additionally, 381 (non-nurse) healthcare professionals were observed for hand hygiene compliance. Compliance with hand hygiene and proper glove use ranged from 9 to 25 %. Survey responses suggested that poor compliance with hand hygiene in the ICU was secondary to multiple issues including ineffective communication of infection control recommendations, insufficient promotion of hand antisepsis, and a deficiency of infection control education [55]. Poor compliance with hand hygiene was similarly observed by Kaplan et al. in a tertiary care American hospital [81]. Physician compliance with hand hygiene was 19 %, while compliance by the nursing staff was 63 %. Greater compliance with hand hygiene was observed among the nursing staff with a 1:1 bed to sink ratio than those with a greater bed to sink ratio (76 % vs. 51 %) [81].

Efforts to improve hand hygiene both in the ICUs and hospital-wide likely require simultaneous interventions on multiple levels. In a study by Bischoff et al. where alcohol-based hand sanitizers were introduced to an ICU, the greatest increment in hand hygiene compliance was observed when the hand sanitizer to healthcare worker ratio went from 1:4 to 1:1, thereby underscoring the importance of accessibility [82]. As such, the CDC now suggests promoting alcohol-based hand sanitizer access both by bedside dispensers and healthcare worker pocket-sized dispensers [54]. Pittet and colleagues improved overall compliance with hand hygiene by implementing a hospital-wide program with special emphasis on bedside, alcohol-based hand disinfection. The campaign ran from December 1994 to December 1997 and consisted primarily of hand hygiene promotion through large, conspicuous posters promoting hand hygiene throughout patient care areas. The project was supported and heavily promoted by senior hospital management. Additionally, alcohol-based handrub solutions were distributed in large amounts, mounted on beds/walls, and given to healthcare workers to encourage pocket carriage for convenience of use. During this time frame, seven institution-wide hand hygiene observational surveys were performed twice yearly. Additional measures included hospital-acquired infection rates, the rate of MRSA infections, and overall consumption of handrub disinfectant. In this 3-year study, 20,000 opportunities for hand hygiene were observed. Compliance with hand hygiene improved from a baseline of 44 % in 1994 to 66 % in 1997. Of note, hand hygiene improved markedly among nursing staff but remained poor for physicians. Additionally, over the study period, the overall prevalence of hospital-acquired infections decreased from 16.9 to 9.9 %, MRSA transmission rates decreased from 2.16 to 0.93 episodes per 10,000 patient days, and the consumption of alcohol-based hand rub increased from 3.5 to 15.4 L per 1000 patient days [109]. Unfortunately, as multiple interventions were employed simultaneously, the relative effect of each component was difficult to properly assess. Thus, although the most efficient and effective means for sustained improvements in hand hygiene compliance have yet to be defined, measures should at least include efforts that stress increased use of accessible, easy to use, medicated hand hygiene products, coupled with a hospital-wide,

administration-supported, high-priority hand hygiene educational and promotional campaign.

2.1 Hand Hygiene Bundles

Bundles are commonly used multimodal approaches in infection prevention practice that aim to improve patient care and outcomes. They combine several interventions concurrently in order to optimize outcomes more than any one intervention could achieve alone. Possible components of a hand hygiene bundle include administrative support, education and training, availability of hand hygiene resources (e.g., hand sanitizer, soap, etc.), and ongoing monitoring and feedback of hand hygiene compliance [110]. One commonly used bundle that is promoted by the WHO includes administrative support toward improved hand hygiene, access to alcohol-based hand rub (ABHR), performance feedback, education, and reminders [111]. Several studies have assessed the use of bundles in order to improve hand hygiene compliance. A recent meta-analysis reviewed the literature with the aim to assess utility of hand hygiene bundles [112]. Forty-six studies were included in the final analysis. There were 39 quasi-experimental, four cluster-randomized, and two randomized controlled trials. Two bundles were associated with improved hand hygiene compliance. One bundle included education, reminders, feedback, administrative support, and access to ABHR, while the other included education, reminders, and feedback. Interestingly, increasing the number of interventions in a hand hygiene bundle was not associated with improved compliance. This review was limited by study heterogeneity. Furthermore, most studies were quasi-experimental in design, which are subject to bias. Robust randomized controlled trials assessing hand hygiene bundles are lacking. Currently underway is a multicenter randomized controlled trial with the aim to identify an optimal hand hygiene bundle [113]. Combinations of three interventions (hand-hygiene point-of-use reminder signs to serve as an environmental cue to action, individual hand sanitizers, and healthcare worker hand cultures) will be assessed.

2.2 Emerging Technologies for Monitoring Hand Hygiene Compliance

Monitoring of hand hygiene provides important information about baseline and ongoing rates of compliance among healthcare workers. Several different methods of monitoring have been tried. Direct observation is the traditional method of monitoring and provides detailed information about adherence to the various components of hand hygiene (e.g., proper technique and compliance before and after patient contact). However, the reliability of direct observation is limited by observer bias as well as the Hawthorne effect [114, 115]. This practice is also time consuming and expensive to carry out. The use of novel hand hygiene technology has become a recent topic of interest and represents a possible alternative to direct observation. Measuring product consumption and electronic monitoring systems have been studied. Boyce recently published a thorough review of these emerging technologies [116]. Measurement of product consumption is accomplished via volume or weight of product used or amount of product purchased. Most studies have shown a direct relationship between amounts of product consumed and observed compliance rates [76, 117–119]. However, several other studies have shown no correlation between product consumption and observed hand hygiene rates [120, 121]. One prospective observational study compared direct observation, product usage, and electronic counting devices as methods of monitoring in a tertiary care hospital 40-bed ICU in Brazil. There were 2249 opportunities for hand hygiene observed with an overall compliance rate of 62.3 %. Direct observation did not correlate with the amount of product used. The authors concluded from this study that direct observation is an inaccurate method of monitoring [120]. Another quasi-experimental study by Morgan et al. similarly concluded that direct observation did not correlate with dispenser counts [121]. Despite this conflicting data, monitoring of product usage is likely to be a useful adjunct to monitoring by direct observation. Monitoring of product usage is less time consuming and less labor intensive, but also provides less detail about each episode. Once baseline product usage for an institution is established, trends can be followed.

Product use can also be monitored with electronic counting devices. These devices record a hand hygiene event every time sanitizer is dispensed. They supply additional important data, including frequency of use, and specific date, time, and location of use. One quasi-experimental study suggested that electronic counting may be a better method of monitoring than direct observation. Over a period of 30 weeks, 424,682 dispenser counts, 338 h of human observation, and 1783 room entries were recorded. Hand hygiene rates were monitored before and after feedback intervention, which included posters displaying unit-specific compliance rates and educational sessions for healthcare workers. Rates significantly increased according to electronic counters (average count/patient day increased 22.7 in the NCICU and 7.3 in the CCU), but were not significantly changed according to direct observation [121]. Larson et al. studied hand hygiene compliance (with the use of electronic counting devices) in response to changes in the hospital's organizational culture [122]. In this quasi-experimental study in two mid-Atlantic hospitals (one hospital received the intervention, while the other served as the control), 860,567 hand hygiene events were recorded over a period of 8 months. The intervention implemented in the study hospital included establishment of leadership support

and role modeling of proper hand hygiene, positive deviance, and feedback to units of current compliance rates. While the hand hygiene rate increased in both hospitals, the difference was greater in the intervention hospital. In addition to improvements in hand hygiene, rates of VRE infections were significantly reduced in the intervention group compared to the control group (85 % vs. 44 %, respectively) [122]. Other studies demonstrated that counting devices provide useful information about patterns of sanitizer use [123, 124]. For example, higher rates of sanitizer use outside of patient rooms than inside patient rooms were recorded [123]. Touch-free dispensers were preferred over manual dispensers [124].

Other technologies, such as dedicated hand hygiene systems and real-time location devices, target hand hygiene at the individual level. Marra et al. conducted a two-phase trial [125]. The first phase assessed baseline rates of hand hygiene using an electronic counting device. The second phase used real-time feedback with a wireless identification device (badge) that flashes red when the healthcare worker approaches the patient bed and has not performed hand hygiene and flashes green when hand hygiene has been performed. There was a significant increase in hand hygiene after implementation of the real-time feedback technology (74.5 episodes/patient day prior to intervention vs. 90.1 episodes/patient day during intervention) [125]. Another two-phase study used real-time feedback in the form of three consecutive beeps and the prerecorded voice prompt, "Please wash your hands," when healthcare workers failed to comply with hand hygiene upon entering or exiting a patient room. Hand hygiene improved from 36.3 % during phase 1 (prior to intervention) to 70.1 % during phase 2 (after intervention) [126]. Other studies reported similar improvements in hand hygiene rates after implementation of feedback technology [127, 128].

Another novel hand hygiene technology is real-time location systems. These systems use technologies such as Wi-Fi, active radio-frequency identification (RFID), infrared, and ultrasound to communicate information from special badges worn by healthcare workers. They have the advantage of being able to locate individual healthcare workers and the dispensers they access. This data is communicated back to a central server for real-time analysis [116]. Pineles et al. compared direct observation of hand hygiene to an RFID system. When compared to recorded data by the RFID system, direct observation was only 52.4 % accurate [129].

Video monitoring has also been used to assess healthcare worker hand hygiene compliance. Armellino et al. used video monitoring as a way to remotely assess hand hygiene in a medical ICU prior to and during a feedback period. Hand hygiene rates were 6.5 % during the 16-week pre-feedback period and 81.6 % during the 16-week post-feedback period. More importantly, the increase was maintained through 75 weeks at 87.9 % [130]. This study was extended to the surgical ICU and achieved similar results [131]. Video monitoring, similar to direct observation, requires significant man-hours, but may have the advantage of improved accuracy.

Possible barriers to implementing these technologies include upfront and maintenance costs, and healthcare worker buy-in. While these new technologies may improve hand hygiene monitoring accuracy and healthcare worker compliance rates, they continue to have shortcomings. They do not provide the level of detailed monitoring achieved by direct observation, such as hand hygiene technique, and hand hygiene practices prior to aseptic procedure or when hands are soiled.

2.3 The Use of Gloves and Gowns to Limit Cross-Transmission of Hospital-Acquired Pathogens

Gloves should be worn to prevent healthcare worker exposure to blood-borne pathogens and to prevent contamination of hands with drug-resistant pathogens during patient care activities. Nevertheless, even with proper glove use, hands may become contaminated during the removal of the glove or with micro-tears that allow for microorganism transmission [132]. Glove use should not be used as a substitute for hand hygiene. The promotion of glove use may increase compliance with hand hygiene protocols. A recent study by Kim and colleagues observed the rate of hand disinfection with glove use and patient isolation [133]. In this prospective, observational study, hand hygiene and glove use compliance rates were measured in two ICUs of a tertiary care hospital. Over 40 h of observation and 589 opportunities for hand disinfection were noted. Overall hand hygiene compliance was 22 %. The investigators found a statistically significant, positive association between glove use and subsequent hand disinfection (RR 3.9). Isolation precautions did not significantly increase hand hygiene compliance. For infection control purposes, glove use should be promoted as a means of limiting hand contamination with drug-resistant pathogens such as MRSA and VRE. Additionally, glove use and hand hygiene should be promoted concurrently.

2.4 Gowns

Gowns have been used as part of contact precaution protocols to limit the spread of hospital-acquired pathogens. Several studies have documented colonization of healthcare worker apparel and instruments during patient care activities without the use of gowns [134–136]. One study by Boyce et al. demonstrated the efficacy of disposable gowns in the prevention of HCW clothing contamination [136]. In another study, Srinivasen et al. prospectively measured the effect of gown and glove use in a 16-bed medical ICU of a tertiary care medical center. Over a 3-month period, all admissions

to a medical ICU were screened for VRE by perirectal swab. Patients who were culture positive for VRE were isolated by hospital policy, requiring the use of gown and glove for patient care. For the following 3 months, precautions were changed to glove use alone. The VRE acquisition rate was 1.8 cases per 100 patient days at risk in the gown/glove group and 3.78 per 100 patient days during glove use alone [137].

Not all studies, however, support the routine use of gowns for infection control measures. In addition, with regard to the endpoint of colonization and cross-transmission, there may be little incremental benefit to gown use over proper glove use and hand hygiene alone. Pelke et al. studied the effect of gowning in a neonatal intensive care unit over an 8-month time frame employing an alternating 2-month gowning and non-gowning cycles. The outcomes of interest were colonization patterns, necrotizing enterocolitis, respiratory syncytial virus, other hospital-acquired infections, mortality, and handwashing. The investigators failed to document any significant difference between the gowning and non-gowning cohorts with respect to the rates of bacterial colonization, infection type, or mortality. In addition, no significant difference in hand hygiene practice was observed [138].

Other investigators have compared gown use in addition to gloves and the effect on hospital-acquired transmission of VRE. Slaughter et al. compared the universal gloving versus universal gown and glove use on the acquisition of VRE in a medical intensive care unit. This prospective study involved 181 consecutive admissions. Half of the 16-bed ICU was designated for universal gown and glove use during patient care activities, and the other half was universal gloving for patient care activities. Rectal surveillance cultures were taken daily from patients along with monthly environmental cultures of bed rails, bedside tables, and other common objects in patient rooms. The investigators found no superiority in the universal use of gowns and gloves versus use of gloves only in preventing the rectal colonization of VRE in a medical ICU cohort [102]. Trick and colleagues compared the impact of routine glove use versus contact isolation on the transmission of multidrug-resistant bacteria in a skilled nursing home environment [139]. Over an 18-month period, all residents admitted to the skilled care unit of an acute and long-term care facility were randomly allocated to two different contact isolation precautions (gown and glove use) vs. routine glove use during patient care. No differences were observed in the transmission of antimicrobial-resistant bacteria, including MRSA, VRE, and extended spectrum beta-lactamase producing *K. pneumonia* and *E. coli* between the two study groups. Of note, greater compliance with proper glove use and hand hygiene was seen in the routine glove use section [139]. Harris et al. conducted a cluster-randomized trial among 20 medical and surgical ICUs. All healthcare workers in the ten ICUs assigned to the intervention groups were required to wear gloves and gowns for all patient contact and when entering any patient room. The ten ICUs in the control groups continued to follow their usual standard of care, which involved contact precautions (gloves and gowns) for patients known to be infected or colonized with multidrug-resistant organisms. Surveillance cultures for MRSA and VRE were performed at the time of ICU admission and at the time of discharge. A total of 92,241 swabs were collected for surveillance cultures from 26,180 patients. Intervention and control ICUs experienced a decrease in patient acquisition of antibiotic-resistant organisms between the baseline and study periods. The difference in change was not statistically significant between the groups, however. In this same study, universal glove and gown use resulted in increased room-exit hand hygiene compliance (62.9% pre-intervention vs. 78.3% post-intervention). Of potential concern, healthcare worker room entry was also decreased (5.24 entries per hour pre-intervention vs. 4.28 entries per hour post-intervention). However, no change in the rate of adverse events was experienced [140]. Thus, although the use of gloves *and* gowns is the convention for limiting the cross-transmission of hospital-acquired pathogens, the incremental benefit of gown use, in endemic settings, may be minimal.

2.5 The Role of Healthcare Worker Apparel in Hospital-Acquired Transmission of Pathogens

Contamination of healthcare worker apparel has been well documented [141–147]. The most commonly isolated organisms include *Staphylococcus aureus*, *Enterococci* (including VRE), and gram-negative organisms. Although evidence that transmission of organisms occur via contaminated clothing is lacking, there remains concern that healthcare worker apparel can act as a fomite for transmission of harmful organisms. The Society for Healthcare Epidemiology of America (SHEA) recently issued expert guidance regarding healthcare worker attire in acute care hospitals [148]. Despite the lack of firm evidence, these recommendations confer low cost and low likelihood of harm. Based on thorough review of the literature and expert opinion, they offered guidance for voluntary adoption of the following policies:

- Bare below the elbows (BBE): This is defined as wearing short sleeves, no wristwatch, no jewelry, and no ties while performing clinical duties. While direct evidence of transmission of organisms from clothing to patients is lacking, this practice is supported by biological plausibility and low risk of harm, according to the authors.
- White coats: If white coats are used, facilities should provide access to two or more coats with easy access to on-site laundering. Hooks should also be provided by the facility as a place where white coats can be hung during patient contact.

- Frequency of laundering: Clothes that come into contact with patients should be laundered daily, while white coats should be laundered at least weekly and when soiled. Preferably, items laundered at home should go through a hot-water wash cycle (with bleach if feasible), followed by a dry cycle. Less frequent laundering of clothing may be indicated for healthcare workers who engage in direct patient contact less often.
- Footwear: For healthcare worker safety, shoes with closed toes, low heels, and nonskid soles should be worn. This practice also confers less risk of exposure to blood, other potentially infectious materials, and injuries due to sharp objects.
- Identification: Identification badges should be worn by healthcare personnel and be clearly visible at all times for identification and security purposes.
- Other recommendations: Equipment used on multiple patients, such as stethoscopes, should be cleaned between patients. No other recommendations were made on additional personal items such as cellular phones, pagers, or other clothing items. In general, any item that comes into contact with multiple patients should be cleaned in between patients.

3 Contact Precautions

Contact precautions prevent spread of organisms from an infected patient through direct (touching the patient) or indirect (touching surfaces or objects that that been in contact with the patient) contact. This type of precaution requires the patient either be placed in a private room or be cohorted with a roommate with the same organism. Healthcare workers should don gloves upon entering the room. After patient care or environmental contact, the gloves should be removed and hand hygiene should be performed prior to leaving the room. In addition, the use protective gowns have been advocated to decrease the risk of healthcare worker garment contamination. Patient care items used for a patient in contact precautions, such as a stethoscopes and blood pressure cuffs, should not be shared with other patients unless they are properly cleaned and disinfected before reuse. Patients should be restricted to the isolation room [150].

Contact isolation is recommended for diarrheal illnesses of infectious origin and for infections with *C. difficile*. Traditionally, contact precautions have also been recommended for patients with drug-resistant pathogens such as MRSA, VRE, and multidrug-resistant gram-negative rods. However, controversies with the use of contact precautions exist.

3.1 Controversies in Contact Precautions

Effectiveness of contact precautions has been exhibited in outbreak situations [151–153]. Extrapolation of these results has led to the use of contact precautions as a control measure for transmission of multidrug-resistant organisms, such as MRSA, VRE, and multidrug-resistant gram-negative rods, in healthcare settings. While some studies have documented reduced rates of transmission of drug-resistant organisms when contact precautions are used, others fail to show this association [140, 161–163]. In addition to conflicting outcomes, well-designed, robust studies are lacking.

Several studies have noted suboptimal compliance with contact precautions. A large prospective cohort study analyzed compliance with various components of contact isolation practices, including hand hygiene prior to donning gloves, gowning, using of gloves, doffing of gown and gloves, and hand hygiene after removal of gown and gloves. Out of the 1013 healthcare workers observed, only 28.9 % adhered to all components of contact precautions [161]. Another prospective observational study involving a 900-bed tertiary care teaching hospital observed 73 % overall compliance with routine gown use. Specifically, healthcare workers were 76 % compliant, while visitors were 65 % compliant [162]. On the other hand, it has been argued that gown use may actually improve hand hygiene compliance. Golan et al. studied this hypothesis with an interventional study in two ICUs in the same tertiary care hospital. The intervention ICU eliminated the use of gowns for contact precautions, while the other ICU continued with the usual use of both gowns and gloves for contact precautions. Of concern, a very low rate of overall hand hygiene compliance was observed (10.1 % before patient care, 35.6 % after patient care, and only 5 % both before and after patient care). Hand hygiene compliance was no different between the intervention and control groups [163]. Another observational study demonstrated improved rates of hand hygiene on exiting the room of patients on contact precautions (63.2 %) vs. patients not on contact precautions (47.4 %), $p < 0.001$ [164]. Notably, a recent prospective cohort study found that as the burden of isolation increased from ≤20 to >60 %, hand hygiene compliance upon room entry decreased from 43.6 to 4.9 % [161].

Of some concern, adverse events associated with the use of contact precautions have been documented. In a prospective cohort study, Saint et al. reported in a prospective cohort study that patients on contact precautions are examined by the attending physician less often than their non-isolated controls (35 % vs. 73 %, respectively) [165]. In 2009, Morgan et al. conducted a review of the literature on adverse outcomes related to contact precautions. Four main outcomes were recognized. Isolated patients experienced less contact with healthcare workers, delays in care and increases in adverse events, increased anxiety and depression, and more dissatisfaction with care [164]. Since that time, several other reports have reinforced these results. A prospective observational study reported that patients on contact precautions had 36.4 % fewer hourly healthcare worker visits and 17.7 % less patient contact time with healthcare workers. These patients also had fewer outside visitors. Another study compared 150

patients on contact precautions to 300 controls. The patients on isolation were more likely to experience preventable adverse events, such as falls and pressure ulcers, experience less satisfaction with care, and have less physician progress notes [166]. Another study surveyed 1876 adult patients. Those on contact precautions had higher depression and anxiety scores [167]. Additionally, patients on contact precautions experience more medication errors, such as erroneous insulin and anticoagulant administration [168].

4 Measures to Control Hospital-Acquired Outbreak of Drug-Resistant Pathogens

Data published by the CDC report that more than 70 % of bacterial pathogens implicated in hospital-acquired infections are resistant to at least one commonly used anti-infective [169]. In addition, current evidence suggests that the proportion of MRSA and VRE attributable to cross-transmission is significant. Transmission of clonal MRSA strains within a healthcare setting has been confirmed by pulsed-field gel electrophoresis and has occurred in various healthcare settings including general hospital wards, neonatal intensive care units, and surgical intensive care units [155, 170–178]. Similarly, the clonal transmission of VRE within healthcare settings has been documented via molecular typing [179–189].

There is no one size fits all approach to the control of hospital-acquired drug-resistant pathogens such as MRSA or VRE. The literature is replete with reports of intervention and programs to limit the spread of drug-resistant pathogens. These examples, occurring in diverse patient populations such as hospital wards, intensive care units, and neonatal units, typically involve different combinations of multiple interventions such as surveillance cultures, pulsed-field gel electrophoresis typing of isolates, patient isolation, cohorting, gloving, gowning, antibiotic restriction, and healthcare worker decolonization [10, 190–195]. The best approach for controlling the hospital-acquired spread of pathogens such as MRSA or VRE should take into account the frequency of transmission of hospital-acquired infection, the reservoirs, the patient risk factors, and the resources of the healthcare system for implementation of varied infection control measures.

5 Screening for Asymptomatic Patient Colonization with Drug-Resistant Pathogens

As the incidence of both patient infection and colonization with drug-resistant pathogens such as MRSA or VRE has increased, the management of this phenomenon has evolved. Aggressive strategies include screening to detect asymptomatic carriers and the strict use of isolation measures to control spread. Nevertheless, there has been much debate about the rationale and efficacy of this practice to control the endemic spread of potential hospital-acquired pathogens.

In the latest guidelines by the Society for Healthcare Epidemiology of America (SHEA) for the prevention and spread of antibiotic-resistant pathogens, the use of active surveillance cultures to identify the reservoirs of MRSA and VRE is strongly recommended [196]. The ultimate goal of active surveillance is to identify every colonized patient so that infection control interventions such as contact isolation and cohorting can be implemented to reduce the risk of cross-transmission. As per the SHEA guidelines, these active surveillance cultures are indicated at the time of hospital admission for patients at high risk for carriage of MRSA and/or VRE [196–201]. For patients with ongoing or prolonged hospitalization, or high risk for VRE or MRSA carriage due to hospital location, underlying comorbidities, and concurrent antibiotic therapy, periodic re-culturing is recommended, typically on a weekly basis [176, 187, 202–209]. Furthermore, for facilities with high endemic rates of VRE or MRSA, as determined by surveillance of high-risk patients, an institution-wide survey should be conducted so that these patients are identified and placed in either contact isolation or cohorted [196].

However, a recently published review of isolation policies by the British National Health Service highlighted the strong evidence for the effectiveness of different isolation and screening policies for MRSA [210]. Data were extracted from articles reporting infection control mechanisms, policies, and interventions for MRSA-related outcomes, including colonization or infection. From 4382 abstracts, 254 full article appraisals were made with 46 papers included in the final review. Of the 46 studies, 18 included the use of isolation wards, 9 used nurse cohorting, and 19 involved other isolation policies including multiple combinations of different interventions such as patient cohorting in single or multiple occupancy rooms, strict use of gown, glove and mask, changes in antibiotic formulary, screening on admission and weekly thereafter, prompt patient discharge, mupirocin for decolonization, hand hygiene education with and without feedback to healthcare workers, and antibiotic restriction. Although the review concluded that concerted efforts, including isolation, can reduce the rates of MRSA in both endemic and epidemic settings, several other findings were noteworthy. The majority of the studies had multiple interventions and major methodological weaknesses such as lack of measures to prevent bias, the absence of consideration for confounding, and inappropriate statistical analysis. As such, the quality of evidence in many studies was considered weak, many alternative and plausible explanations for the reduction in MRSA could not be excluded, and the role and impact of isolation measures were not assessed by well-designed studies.

At least one recently published, well-designed, prospective study evaluated the efficacy of single room and cohort isolation for MRSA in the intensive care unit setting [211]. In this 1-year analysis conducted in the intensive care units of two teaching hospitals, MRSA screening was performed both on admission and then weekly for all patients. During the first 3 months and the last 3 months, all MRSA-positive patients were moved either to a single occupancy isolation room or cohorted with other MRSA-positive patients. During the middle 6-month period, MRSA-positive patients were not placed in isolation or cohorted unless they were co-colonized with another multidrug-resistant pathogen. Patient characteristics, hand hygiene compliance, and MRSA acquisition rates were similar in the periods when patients were moved and not moved. Using Cox proportional hazard modeling to control for confounders such as gender, age, APACHE II score, antibiotic use, number of intravascular catheters, and colonization pressure, no significant reduction in MRSA acquisition was observed between the two groups [211].

The use of strict isolation practices may have a detrimental impact on the process and quality of patient care. Evans et al. prospectively observed surgical patients in both the ICU and on a general surgical floor. In both the ICU and surgical floor, surgical patients on contact isolation had fewer healthcare worker visits and less contact time overall despite a higher severity of illness as measured by APACHE II score [212]. Stelfox et al. studied the quality of medical care received by patients isolated for MRSA-related infection control precautions using a case control study design. Although isolated and control patients had similar baseline characteristics, isolated patients were twice as likely as non-isolated patients to experience adverse events during their hospitalization. These adverse events included supportive care measures and process of care measures such as days with incomplete or absent vital signs and days without documented nursing and physician progress notes. Additionally, patients on MRSA contact isolation expressed greater dissatisfaction with the quality of their treatment [166]. Similarly, Saint and colleagues observed, in a prospective cohort study of two in-patient medical services, that patients on contact isolation were half as likely to be examined by an attending physician as non-isolated patients [165].

Contact isolation may have a detrimental psychological impact on patients. One cross-sectional matched case control study compared contact isolated versus non-isolated elderly patients [213]. The level of depressive and anxiety symptoms exhibited by the contact isolation group exceed that of the noncontact isolation group. Catalano et al. prospectively studied the impact of contact isolation on anxiety and depression in non-critically ill hospitalized patients [214]. Patients on contact isolation for either MRSA or VRE were compared to other hospitalized patient with infectious diseases not requiring isolation. All patients were evaluated with the Hamilton Anxiety and Depression Rating Scale at baseline and then later during the hospital course. Although no significant differences in baseline anxiety and depression scores were noted, for patients in contact isolation, statistically significant higher scores on both scales were reported later during the course of hospitalization.

Thus, the optimal strategy for control of endemic, resistant pathogens such as MRSA or VRE is yet to be defined. Aggressive measures involving surveillance cultures for colonized patient reservoirs may not effectively reduce the rate of pathogen cross-transmission. Additionally, surveillance cultures with consequent the implantation of isolation measures may have the impact of increased patient depression and anxiety, and may be detrimental to the both the process and quality of care.

6 Antibiotic Control Programs and Surveillance for Hospital-Acquired Infections

The implications of widespread antibiotic use, including the impact on public health, are beyond the scope of this chapter. The reader is referred to other chapters within this textbook for further information on the topic. Although the degree to which antibiotic pressure directly contributes to the cross-transmission of hospital-acquired infections remains poorly defined, several studies and observations are worth mentioning. Harbath and colleagues prospectively studied surgical site infections in cardiovascular surgical patients. In this cohort, prolonged antibiotic prophylaxis with cephalosporins was an independent risk factor on logistic regression analysis for infections with cephalosporin-resistant gram-negative rods [215]. Additionally, in a prospective, non-randomized, cohort study in a neonatal ICU, a change to a new empiric antibiotic regimen resulted in a decrease in colonization or infection by gram-negative organisms resistant to the standard or prior empiric regimen [216]. Donskey and colleagues showed that enteric VRE colonization was significantly associated with colonization pressure, presence of feeding tube, and cephalosporin use [217]. Similarly, MRSA colonization has been associated with antibiotic use. A significant risk factor for prolonged MRSA colonization, as defined by multivariate regression analysis, was fluoroquinolone use [218]. Additionally, using an ecologic study design, investigators from Belgium reported a direct association between fluoroquinolone use and MRSA infections [219]. Consideration should be given to antibiotic restriction and control programs in the event of elevated rates of hospital-acquired drug-resistant pathogens.

According to the Society for Healthcare Epidemiology of America (SHEA), antimicrobial stewardship refers to coordinated interventions designed to improve and measure the appropriate use of antimicrobials by promoting the selection

of the optimal antimicrobial drug regimen, dose, duration of therapy, and route of administration [220]. All healthcare institutions in the United States are urged to adopt antimicrobial stewardship programs. The goal of these programs is to improve clinical outcomes by optimizing antimicrobial use in order to minimize toxicity, reduce adverse events, and reduce selective pressure that leads to antibiotic resistance. In 2012, SHEA, the Infectious Diseases Society of America (IDSA), and the Pediatric Infectious Diseases Society (PIDS) issued a joint policy statement regarding antimicrobial stewardship [221]. Several recommendations are given.

First, antimicrobial stewardship programs should be required through regulatory mandates (through a combination of state and federal mandates, and via the Centers for Medicare and Medicaid Services (CMS)). However, objectives should be flexible enough so that resource-limited facilities are able to maintain participation in such programs. Requirements of a program should include:

- A multidisciplinary antimicrobial stewardship team, which is physician directed and has at least one team member trained in antimicrobial stewardship. At the least, the team should include a physician, a pharmacist, a clinical microbiologist, and an infection preventionist.
- A medication formulary limited to non-duplicative antibiotics of clinical need.
- Institutional guidelines for the use of antibiotics for management of common clinical syndromes.
- Methods for detecting and eliminating the use of antibiotics in a manner that is redundant, inappropriate, or inadequate (e.g., the use of antibiotics for the treatment of nonbacterial illness and the use of antibiotic regimens that are either too broad, not broad enough, or not appropriately targeted for the pathogen).
- Processes for monitoring antibiotic use for internal benchmarks.
- Periodic distribution of facility-specific antibiograms to clinicians.

In addition, CMS should require institutions to report to the National Healthcare Safety Network's (NHSN) Antimicrobial Use and Resistance option of the Medication-Associated Module, conduct prospective surveillance and concurrent interventions to optimize antimicrobial use, establish national benchmarking of antimicrobial use at the institutional level based on acuity of care and patient mix, and report other indicators of effective antimicrobial use such as incidence rates of drug-resistant organisms and *C. difficile* infections.

Second, validated antimicrobial stewardship interventions do not exist for ambulatory healthcare settings. Therefore, pilot projects should be designed to develop and implement antimicrobial stewardship interventions in these settings. National organizations, such as the Agency for Healthcare Research and Quality (AHRQ), CMS, National Institutes for Health (NIH), and the Centers for Disease Control and Prevention (CDC) should provide funding for such projects. Suggested areas of research include integration of clinical decision support into electronic health records and e-prescribing systems. Once validated, interventions should become CMS requirements.

Third, mechanisms should be put into place to educate physician trainees (e.g., medical students, residents, and fellows) about antibiotic resistance and antimicrobial stewardship. Furthermore, practicing clinicians should receive education as well. Educational materials can be distributed through specialty societies, the FDA, and individual institutions, for example.

Fourth, there should be a national system for collecting antimicrobial use data, which can then be used to benchmark institutions. The data could potentially be used as part of an incentive-based payment system.

Fifth, research on antimicrobial stewardship is needed in order to understand antimicrobial resistance and how interventions affect it. This is best accomplished via translational research. Research should focus on:

- Development of a standard definition of appropriate and inappropriate antimicrobial use, measures of use, and the factors that contribute to misuse. In addition, standardized data collection tools should be developed for purposes of measurement and interpretation of antimicrobial use.
- Determination of the most effective and cost-efficient means of implementing antibiotic stewardship programs in various settings, using robust study design.
- Development and validation of process and outcome measures that allow comparison of antimicrobial use within and across healthcare settings. Measures may include surrogate markers of effective and appropriate antibiotic use, such as rates of infections due to drug-resistant organisms and *C. difficile* infections, adverse effects of antibiotics, and hospital/ICU length of stay.
- Understanding how generic versus trade name antimicrobial agents affects use.
- Evaluation of the impact of rapid diagnostic tests and biomarkers, such as procalcitonin, on the use of antibiotics, and whether or not unnecessary antibiotic use (e.g., for viral infections) is decreased.

7 Conclusion

The prevalence of hospital-acquired, antibiotic-resistant pathogens has increased significantly over the last 20 years. Hospital infection control programs are seen as increasingly important for the control of antibiotic-resistant organisms. Strategies to control the spread of hospital-acquired infections by drug-resistant pathogens are multiple. The patient, the healthcare

worker, and the environment are reservoirs for drug-resistant pathogens. For high-risk patients colonized with MRSA, such as surgical candidates and those in intensive care units, decolonization with nasal mupirocin should be considered. Patients colonized with resistant pathogens such as MRSA, VRE, and drug-resistant gram-negative rods can contaminate the environment. As such, all healthcare facilities should develop policies for the terminal and periodic disinfection of patient care areas and environmental services. Cross-transmission of hospital-acquired pathogens by the hands of healthcare workers has been well documented. Meticulous hand hygiene should be practiced with medicated handwashing agents (alcohol, chlorhexidine gluconate, triclosan) that are bactericidal and effectively reduced bacterial counts on the hands. Measures to promote hand hygiene compliance should include efforts that stress increased use of accessible, easy to use, medicated hand hygiene products, coupled with a hospital-wide, administration-backed, high-priority hand hygiene campaign. Glove use is beneficial in limiting the contamination of healthcare worker hands but is not a substitute for hand hygiene. Concerns about the contamination of personnel clothing with hospital-acquired pathogens has led to the use of gowns for patients in contact isolation. The incremental benefit of gowns and glove use may be minimal. Transmission-based precautions are useful for the control of hospital-acquired infections and include contact, airborne, and droplet precautions. Aggressive surveillance for asymptomatic reservoirs may be of value but is not without controversy including questions about efficacy and effect on quality of care. Other considerations for an infection control program include antibiotic control programs and surveillance systems for infections with hospital-acquired pathogens. This type of surveillance is essential for establishing endemic rates, defining outbreaks, and developing institution-specific antibiograms. In the end, the purpose of a hospital infection surveillance program is to define endemic rates, recognize outbreaks, and obtain data of value in recognizing the extent and causation of the infections. This data is later applied for the planning and implementation of risk reduction policies and interventions.

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