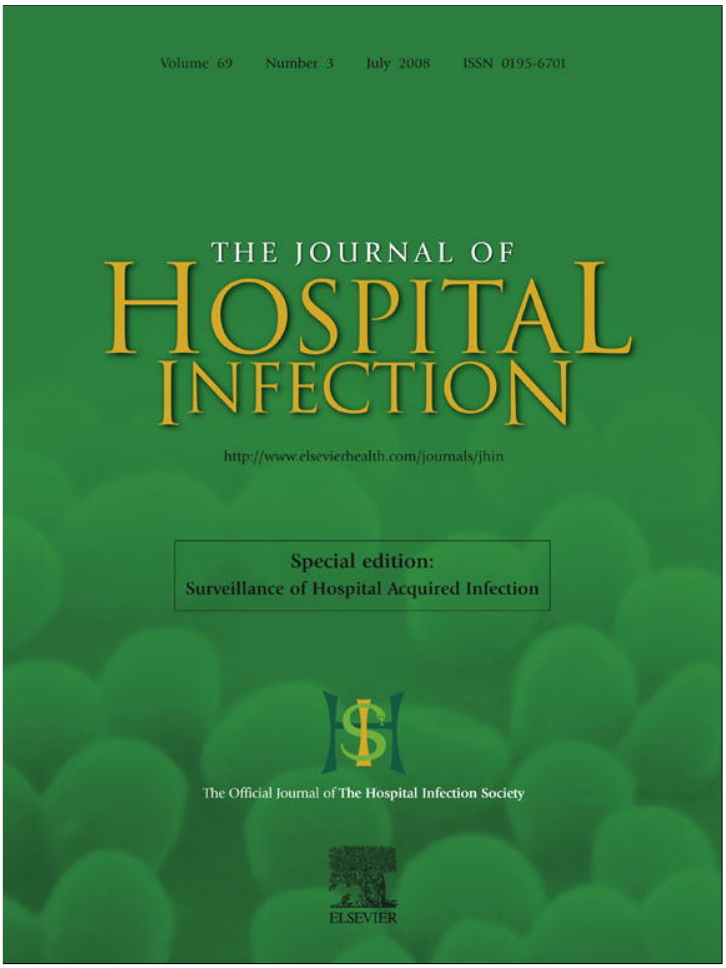

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REVIEW

Prevention of hospital-acquired infections: review of non-pharmacological interventions

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KEYWORDS
Nosocomial infection; Hand washing; Hospital cleaning; Nutrition; Urinary tract infections; Ventilator-associated pneumonia; HEPA filtration

Summary Hospital-acquired (nosocomial) infections (HAIs) increase morbidity, mortality and medical costs. In the USA alone, nosocomial infections cause about 1.7 million infections and 99 000 deaths per year. HAIs are spread by numerous routes including surfaces (especially hands), air, water, intravenous routes, oral routes and through surgery. Interventions such as proper hand and surface cleaning, better nutrition, sufficient numbers of nurses, better ventilator management, use of coated urinary and central venous catheters and use of high-efficiency particulate air (HEPA) filters have all been associated with significantly lower nosocomial infection rates. Multiple infection control techniques and strategies simultaneously ('bundling') may offer the best opportunity to reduce the morbidity and mortality toll of HAIs. Most of these infection control strategies will more than pay for themselves by saving the medical costs associated with nosocomial infections. Many non-pharmacological interventions to prevent many HAIs will also reduce the need for long or multiple-drug antibiotic courses for patients. Lower antibiotic drug usage will reduce risk of antibiotic-resistant organisms and should improve efficacy of antibiotics given to patients who do acquire infections.

Introduction

Much of the recent research on nosocomial infections has dealt with the need for new antibiotics, better antibiotic management and better diagnostic techniques to detect infections earlier. Better drug treatment and earlier infection diagnosis can certainly play a major role in reducing morbidity and mortality from hospital-acquired infections (HAIs). However, there are many non-pharmacological interventions that can significantly reduce the incidence of HAIs, but these are often overlooked in practice. This review is not exhaustive and will not attempt mathematical data analysis

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but will examine recent research that examines non-pharmacological interventions for reducing HAIs. It will also include a brief description of the morbidity, mortality and medical costs associated with nosocomial infections, along with a brief discussion of the routes by which HAIs spread.

Methods

A bibliographic search between January 1995 and January 2008 was conducted in databases including PubMed, Medline and Google Scholar. Additional research articles were collected from conference proceedings, books and pre-1995 journal articles as appropriate. Many terms were used in the literature searches including nosocomial, hospital acquired, MRSA (meticillin-resistant *Staphylococcus aureus*), staphyloccoccus, streptococcus, VRE (vancomycin-resistant enterococcus), Clostridium difficile, legionella, klebsiella, tuberculosis, airborne infection, waterborne infection, hand washing, hospital cleaning, urinary catheters, central catheters, haemodialysis, ultraviolet light, HEPA (high-efficiency particulate air) filtration and many others. A total of 160 articles was included in this review. Care was taken to see that a balanced representation of articles was presented.

Results

Morbidity, mortality and economic cost of HAIs

HAIs cause a huge amount of morbidity and mortality. Klevens *et al*. used data from the National Nosocomial Infections Surveillance (NNIS) system, and data from the National Hospital Discharge Survey and the American Hospital Association Survey to estimate nosocomial morbidity and mortality.[1] This study estimated that there were 1 737 125 nosocomial infections in the USA in 2002, of which 561 667 were due to urinary tract infections, 290 485 to surgical site infections, 250 205 to pneumonia, 248 678 to bloodstream infections and 386 090 to other causes.

It is difficult to obtain a precise estimate of deaths from nosocomial infections since patients often die from several causes and infection is often not mentioned on death certificates of patients who die of a combination of a chronic illness (such as cancer) and acute infection(s).[1] Estimated annual deaths in the USA due to HAIs in 2002 was 98 987.[1] In 2005, an estimated 18 650 died in the USA of MRSA infections, of which most were nosocomial.[2] A study of 524 consecutive deaths in a Spanish 800-bed tertiary care hospital reported that 21.3% of the deaths of patients which occurred more than 48 h after admission were due to nosocomial infections.[3]

While it has been long known that HAIs are very expensive to treat, cost estimates of nosocomial infections vary. A US study of 1 355 347 admissions in 55 US hospitals from 2001 to 2006 estimated that each nosocomial infection increased medical costs by $12,197.[4] A French study reported that hospital-acquired sepsis increased medical costs by a mean of €39,500.[5] Various studies have estimated that the average cost of ventilator associated nosocomial pneumonia from US$10,019 to $50,000 per case.[6,7] Hospital-acquired bacteraemia has been estimated to increase medical costs in a Belgian study by an average of €12,853 and in a Michigan study by $34,508.[8,9] A British study reported that the average increased medical cost for each central venous catheter infection was £6,200.[10]

Infection routes for HAIs

Traditionally, it has been believed that most nosocomial infections, with a few exceptions such as tuberculosis and Aspergillus and viruses like respiratory syncytial virus (RSV), influenza, rhinoviruses and coronaviruses, are not spread through the air.[11] While a large percentage of HAIs are spread through surface contact (such as hands) or by catheters, intravenous (IV) lines or surgical incisions, many nosocomial infections can also spread through the air. It was previously believed that most pathogenic bacteria could not survive as bioaerosols and spread significant distances to infect patients. However, many airborne pathogenic bacteria are viable but not culturable, and some experts have estimated that as little as 1% of viable bacteria are culturable by standard microbiological techniques.[11,12] For example, Heidelberg *et al*. reported that viable counts of *Serratia marcescens*, *Klebsiella planticola* and *Cytophaga allerginae* in 4-hour-old bioaerosols were, respectively, 48, 73 and 66% of the original counts even though none of the bacteria was culturable on tryptic soy agar plates.[12] Many pathogens present on sneezes evaporate in less than a second into small droplet nuclei of about 2 μm diameter.[13,14] Such small droplet nuclei can remain suspended for hours and travel long distances before settling.[14]

A number of studies have reported airborne transmission of many pathogenic bacteria to humans including MRSA, coagulase-negative staphylococci, *Corynbacterium diphtheriae*, *Neisseria*

meningitidis, *Bordetella pertussis*, Acinetobacter and Pseudomonas.[15–20] A mouse study reported two strains of *Klebsiella pneumoniae* which could infect and multiply in mouse lungs after airborne exposure.[21] Therefore it may be concluded that while many nosocomial bacterial infections are spread by contact or by IV routes, the airborne route is also an important source of many HAIs.[11]

Pathogens from hospital water are another underappreciated and underdiagnosed source of hospital infection.[22,23] Over 30 published studies employing both epidemiology and molecular biology techniques [such as polymerase chain reaction (PCR) and DNA probes] have confirmed that contaminated hospital water sources can cause nosocomial outbreaks from many pathogens including Legionella, Mycobacteria, Pseudomonas, Stenotrophomonas, Serratia, Acinetobacter, Aeronomas and moulds such as Fusarium, Aspergillus and Exophialia.[22,23] Hospital water can also be contaminated with amoebae and viruses.[24] It is estimated that waterborne nosocomial pseudomonas infections kill 1400 annually in the USA.[22] Legionella is found in many hospital water systems and can persist for years. Viable legionella were found in the water systems of 14 of 20 (70%) US hospitals and 17 of 20 (85%) Spanish hospitals.[25,26] Environmental pulsed-field gel electrophoresis studies have confirmed that specific legionella strains can persist for as long as 17 years in hospital water supplies.[27] Viable pathogens can grow in many sources of hospital water including drinking water, hand-washing water, ice, dialysis water, shower water, water in storage tanks and distribution systems, water from decorative pools/fountains, and carpets, furniture, ventilation ducts and building materials that have become wet.

Contaminated environmental surfaces (such as bedside rails) are also an under-recognised source of hospital infections.[28] Many surfaces in hospitals contain viable pathogens such as MRSA and VRE.[28] In rooms of patients with diarrhoea, viable MRSA has been collected from 59% of the room surfaces and viable VRE has been collected from 46% of room surfaces.[29,30] Many strains of MRSA and VRE can remain viable for several weeks to several months on dry surfaces.[31,32]

Infections can also be spread to hospitalised patients via drugs, intravenous solutions, cleaning solutions or by foodstuffs. A review of 2250 HAIs obtained via contaminated substances reported that the most commonly involved items were disinfection materials ($N = 622$ patients), heparin solutions ($N = 451$), red blood cells, clotting factors and other blood products ($N = 333$), albuterol inhalers ($N = 143$), total parenteral nutrition ($N = 109$), propofol ($N = 53$), rantidine ($N = 50$) and ultrasound gel ($N = 36$).[33]

Prevention of HAIs

The remaining part of the results section will concentrate on research on interventions to reduce HAIs. Table I gives a summary of 48 non-pharmacological interventions that have either been proven to reduce nosocomial infections or some level of evidence suggests may be effective.

Hand washing, gloving, gowning and personal items

Frequent and adequate hand washing is the best way to prevent spread of most nosocomial infections. The extreme importance of hand washing has been known since at least 1847, when Dr Ignaz Semmelweis discovered that washing hands before performing obstetric exams on pregnant women reduced childbirth-related infectious mortality from more than 10% to less than 1%.[34] However, rates of hand washing among healthcare providers usually range from only about 20 to 50% per hospital patient encounter, although some studies have reported hand-washing rates as high as 81%.[35–37] Viable pathogens are often found on hands of healthcare providers. Various studies have reported the following pathogens on the respective percentage of healthcare providers' hands: *Acinetobacter* spp. 3–15%, *Clostridium difficile* 14–59%, *Klebsiella* spp. 17%, MRSA up to 16.9%, *Pseudomonas* spp. 1.3–25%, rotavirus 19.5–78.6%, VRE to 41% and yeasts (including candida) 23–81%.[38]

Most studies have reported that increases in hand-washing rates significantly reduce rates of HAIs including MRSA although a few studies have reported negative results.[37,39–45] Alcohol-based hand-washing solutions are generally considered to be more effective than soap and water. Compared with plain soap and water, some studies have reported significantly lower rates of nosocomial infections when alcohol-based solutions or chlorhexidine- or triclosan-based hand-washing agents are used.[36,43,46,47] An Australian hospital study noted a hand hygiene programme that switched from soap to a chlorhexidine/isopropyl alcohol solution reduced MRSA bacteraemia by 57% ($P = 0.01$) and reduced clinical isolates of lactamase-resistant *E. coli* and Klebsiella by 90% ($P < 0.001$).[41] Some studies have also reported that the economic savings that alcohol or chlorhexidine hand-washing solutions provide by reducing nosocomial infections will far more than pay for the cost of the hand-washing solutions.[36,47]

Table I Non-pharmacological hospital infection control strategies which have either been proven effective or some level of evidence suggests may be effective

Class of intervention	Interventions used
1. Hand washing, gowning and personal items	I. Increased hand-washing rates
	II. Alcohol-based and/or antiseptic hand-washing solutions
	III. Disposable gowns, gloves
	IV. Avoiding, regular cleaning or one-patient use of such items as artificial fingernails, rings, stethoscopes, blood pressure cuffs and electrodes
2. Cleaning	I. Better training and feedback for hospital cleaning staff
	II. Bleach may be more effective than other cleaners for such pathogens as *C. difficile*
3. Nutrition	I. Malnutrition common in hospitalised patients and increases risk of nosocomial infection
	II. 'Immunonutrition' enteral and parenteral formulas may reduce infection risk in acutely ill
	III. Probiotics may reduce risk of some infections such as *C. difficile*
4. Administration controls and surveillance	I. Housing patients in separate rooms may reduce nosocomial infection risk
	II. Admission screening or 'search and destroy' protocols for MRSA and other pathogens
	III. Molecular biology methods to detect pathogens on patient, staff and environmental surfaces
	IV. Need for adequate numbers of nurses
	V. Public reporting of nosocomial infections has been proposed as possible method to reduce infections
5. Preventing urinary tract infection	I. Proper catheter cleaning and management
	II. Silver- or nitrofurazone-coated catheters
6. Preventing central venous line and haemodialysis infections	I. Barrier precautions and antiseptic site cleaning when inserting catheters
	II. Subclavian site of insertion: less infection risk than femoral site
	III. Chlorhexidiene- or silver sulfadiazene-coated catheters may reduce infection risk
	IV. Higher rates of infection in temporary catheters vs PTFE grafts or AV fistulas
	V. Dedicated machines for HCV^{+} and HCV^{-} patients
7. Avoiding ventilator-associated pneumonia	I. Use positive pressure ventilation instead of intubation whenever possible
	II. Place patient in semi-erect position
	III. Use enteral instead of parenteral feeding when possible
	IV. Kinetic bed therapy
	V. Subglottic secretion drainage
	VI. Use heat and moisture exchangers vs heated humidifiers
	VII. Oral decontamination with chlorhexidine
8. Avoiding surgical infection	I. Avoiding long or contaminated surgical procedures whenever possible
	II. Clipping rather than shaving surgical sites
	III. Warming surgical patients
	IV. Laparoscopic rather than open abdominal surgery whenever possible
	V. Proper cleaning of surgical instruments
9. Preventing waterborne hospital infections	I. Sterile water for drinking, bathing and procedures
	II. Cleaning shower areas and sinks
	III. Heating water to 50 °C may reduce some pathogens such as Legionella
	IV. UV water treatment may reduce Legionella concentrations
	V. Copper—silver water ionisation systems may reduce pathogen levels
	VI. Regular monitoring of Legionella may or may not be helpful
	VII. Repair water leaks within 24 h
	VIII. Avoid installation of large indoor decorative pools and fountains
10. Air filtration and treatment	I. HEPA filtration reduces airborne levels of many pathogens
	II. Adequate outdoor air infiltration rates
	III. UV-light treatment reduces levels of some, but not all pathogens
11. Preventing spread of tuberculosis	I. Proper mask use when in contact with patients with infectious TB
	II. UV lights and adequate outdoor air infiltration
	III. Negative pressure rooms
	IV. Testing and surveillance of patients and staff

MRSA, meticillin-resistant *Staphylococcus aureus*; HCV, hepatitis C virus; UV, ultraviolet; PTFE, polytetrafluoroethylene; AV, arteriovenous; HEPA, high-efficiency particulate air; TB, tuberculosis.

It is estimated that hand washing with plain soap for 30 s removes most soil and dirt, eliminates about 90% of transient hand flora but a low percentage of resident hand flora.[48] Hand washing for 15 s with a soap containing chlorhexidine or triclosan removes most soil and dirt and about 99.9% of transient flora and about 50% of resident flora. Hand rubbing for 15 s with an alcohol-based gel does not remove soil or dirt, but kills about 99.999% of transient flora and about 99% of resident flora.[48]

Many healthcare providers prefer using alcohol-based solutions instead of soap and water, and compliance rates are generally higher when alcohol-based hand-washing solutions are used.[49] Use of alcohol-based cleaners saves time and these generally abrade and irritate the skin less than antiseptic soaps.[49] However, some people complain that alcohol-based cleaners dry out and crack their skin.[49] Hospitals and healthcare providers may want to experiment with several alcohol or chlorhexidine-based hand cleaners. Soap and water may still have to be used in cases when hands are visibly soiled. In that case, staff and visitors should wash hands carefully for at least 15 s with soap and water.[49] Table II lists six abridged 'golden rules' to improve hand hygiene compliance proposed by Dr Gunter Kampf.[50]

In 2002, the US Centers for Disease Control and Prevention (CDC) published new guidelines for hand hygiene.[51] Major changes of these guidelines over the 1995 guidelines included use of waterless alcohol-based cleaners (unless hands are visibly soiled), prohibition of artificial fingernails and an institutional mandate to provide staff education and develop a multidisciplinary programme to monitor compliance. To measure effectiveness of these new CDC guidelines, an anonymous survey of 1359 staff in 40 hospitals was made after the new guidelines had been in force for a year. This survey found that mean hand-washing rates were only 56.6%, and 45% of the hospitals had no multidisciplinary programme to improve compliance.[51]

It is not certain what type of glove provides the best protection for infection control. Some studies have suggested that latex gloves are somewhat better in preventing penetration of water and virus than vinyl gloves.[52] However, about 3—16% of healthcare workers are sensitive to latex and sometimes experience severe respiratory reactions to it. If latex gloves are used in the healthcare setting, only the powder-free gloves should be used since these release much lower levels of latex allergens than the powdered latex gloves. Nitrile gloves also have good barrier penetration but are more expensive and heavier than either latex or vinyl gloves.[52]

Gowns are often used in rooms of patients with infectious disease. Data on gown use and nosocomial prevention are sparse. One study reported that use of disposable gowns in an intensive care unit (ICU) was associated with a 54% reduction in VRE ($P < 0.01$).[53] Gown use in this study also produced an annual net benefit of $419,346 in the ICU by averting an estimated 58 VRE cases.[54] Another study reported that use of gowns was associated with a modest and insignificant drop in MRSA cases.[55] Rates of gown usage by healthcare providers and staff are generally mediocre, with one study reporting mean gown usage in rooms of patients with contact precautions was only 76% for healthcare providers and 65% for visitors.[56]

Shoe and head covers are often recommended for use in areas containing immunocompromised or surgical patients. Although bacterial pathogens have been collected from shoes, research on the use of shoe covers and/or separate hospital shoes and spread of pathogens has been meagre.[57] One study reported that wearing gowns and shoe covers in bone marrow surgery did not significantly reduce patient infection risk (as measured by antibiotic therapy).[58] An experimental laboratory study involving sham surgery reported significantly lower levels of airborne bacteria when headgear was worn versus no headgear.[59]

Various studies have reported that nosocomial pathogens are present on many items of healthcare providers such as laboratory coats, stethoscopes, blood pressure cuffs, EKG electrodes, pens, finger rings, neck ties, artificial nails and ambulances.[60—68] To prevent spread of nosocomial infections, these items should be disinfected or cleaned regularly. Disposable one-use electrodes

Table II Kampf's six 'golden rules' for hand washing (abridged)[50]

1. Select an alcohol-based hand-cleaning solution that has good skin tolerance.
2. Hand rubs should be easily available. Wall dispensers near the patient may help.
3. Implement teaching and promotion of hand hygiene.
4. Create a hospital budget which covers all costs involved with preventable nosocomial infections. Even a small number of nosocomial infections prevented will outweigh the cost of effective hand hygiene products.
5. Encourage senior staff to set a good example to motivate junior staff.
6. Have adequate staff:patient ratios.

are now available.[63] Sometimes, pieces of equipment such as stethoscopes or blood pressure cuffs are dedicated to one patient only in order to limit spread of pathogens.

Proper cleaning techniques

Proper cleaning techniques and proper cleaning chemicals can also significantly reduce hospital pathogen levels and risk of nosocomial infections. One study utilised a fluorescent marker solution to determine cleaning efficacy of 13 369 surfaces found in 1119 patient care rooms of 23 US hospitals.[69] Terminal room cleaning after patient discharge was able to adequately clean only a mean of 49% of the standardised surfaces, including less than 30% for toilet hand holds, bedpan cleaners, room door knobs and bathroom light switches. Carling *et al*. recommended that hospitals monitor performance of cleaning personnel and provide feedback and training as needed to optimise cleaning effectiveness.[69] Several studies have reported that hospital cleaning personnel often receive little initial training and, after receiving instruction, often do a much better job of eliminating pathogens by their cleaning.[70,71]

An Illinois prospective study reported that following a cleaning educational programme, average rates of cleaning ICU surfaces rose from 48 to 87%. Rates of VRE infection were reduced by 64% [95% confidence interval (CI): 0.19—0.68].[72] A British retrospective ICU study reported that significantly higher rates of MRSA infection were associated with inadequate surface cleaning and nurse understaffing.[73]

Research on chemicals used to clean non-porous surfaces (such as floors, walls, tables etc.) in hospitals and their effects on reducing nosocomial infection has been sparse.[74] In a 2004 literature review, no randomised controlled trials and only four cohort studies could be identified.[74] Three studies detected no significant differences between nosocomial infection rates when comparing surface cleaning with aldehydes, quaternary ammonium compounds, active oxygen cleaners or *ortho*-benzyl *para*-chlorophenol compared with plain detergent solutions. The fourth study reported that use of 1:10 hypochlorite (bleach) solution was associated with a significantly lower rate of *C. difficile* infection in bone marrow patients compared with cleaning with quaternary ammonium compounds.[75] Another study of 17 rooms which housed VRE-positive patients found that 16 (94%) of the rooms' surfaces contained viable VRE before cleaning, but 0 (0%) had viable VRE after thorough cleaning with a 10% bleach solution ($P < 0.001$).[71]

Hydrogen peroxide vapour may be used to decontaminate rooms containing pathogens. A British study compared manual cleaning of rooms (via a protocol compliant with UK standards) with a 5 h protocol using 40 min of 500 ppm hydrogen peroxide vapour to decontaminate rooms.[76] In 10 surgical ward rooms, 89% of 124 swab samples were positive for viable MRSA before manual cleaning, and 66% of 124 matched swabs were still positive for viable MRSA after cleaning. By comparison, in six other surgical rooms, viable MRSA was found on 72% of 85 swabs before hydrogen peroxide treatment, but on only 1% of 85 matched swabs following hydrogen peroxide treatment. During the hydrogen peroxide disinfection, hydrogen peroxide levels in adjacent rooms were no greater than 1 ppm at head height.[76] More study is needed on the safety and efficacy of this hydrogen peroxide vapour technology.

Research is currently underway to use copper-oxide-impregnated textiles and paints in order to prevent spread of infections.[77]

Nutrition and probiotics

Better nutrition can also play a critical role in reducing nosocomial infections. Malnutrition is very common in hospitalised patients. A review of 110 published studies in acute care patients reported that malnutrition ranged from 13 to 78% of all hospitalised patients and 42—91% of hospitalised elderly.[78] Malnutrition was measured by such parameters as weight, weight loss, body mass index, grip strength, respiratory function, nutritional intake and blood levels of albumin, and prealbumin.[78]

Many nutrients play a key role in maintaining immunity including protein, omega-3 fatty acids, vitamins A, B_6, B_{12}, C, D, and E; selenium, zinc, copper and iron.[79] Most of these nutrients become depleted following acute illness.[79] Malnutrition is a major risk factor for infection. A study of 630 hospitalised patients reported that the odds ratio risk of HAIs was 4.98 times as great (95% CI: 4.6—6.4) in severely malnourished patients compared with adequately nourished patients.[80] Other studies have reported that malnourished elderly are significantly more likely to acquire nosocomial infections and are significantly more likely to acquire pneumonia compared with well-nourished elderly.[81,82]

Better nutrition may play a major role in reducing nosocomial infection in acutely ill hospital patients who cannot eat by the regular oral route. In recent years, 'immunonutrition' enteral formulas containing larger quantities of antioxidant vitamins, zinc and other trace metals, omega-3 fatty acids and amino acids like glutamine have become more

commonly used. Meta-analysis has calculated that enteral immunonutrition in hospitalised patients is associated with a 46% lower risk of nosocomial pneumonia (11 studies, $P = 0.007$), a 55% lower risk of bacteraemia (nine studies, $P = 0.0002$), a 78% lower risk of abdominal abscesses (six studies, $P = 0.005$), and a 34% lower risk of urinary tract infections (10 studies, $P = 0.05$) compared with patients receiving standard enteral formula.[83]

Many hospitalised patients develop serious *C. difficile* infections after several antibiotic courses. Probiotic bacteria and yeasts can be helpful in preventing or clearing infections by *C. difficile* and other bacteria. Meta-analysis of 25 studies reported that supplemental *Saccharomyces boulardii*, *Lactobacillus* spp. or *Bifidobacterium* spp. were associated with significantly lower levels of antibiotic-associated diarrhoea.[84] Meta-analysis of six studies indicated that *S. boulardii* was effective in reducing the incidence of *C. difficile* diarrhoea.[84] Yoghurt containing active *Lactobacillus* spp. has been found to be effective in preventing or clearing infections caused by *C. difficile* and VRE in hospitalised patients.[85,86]

Housing patients in separate rooms, pathogen surveillance and 'search and destroy' strategies for nosocomial infections

Housing patients in separate rooms may reduce risk of HAIs. A Quebec observational study of a 14-bed ICU measured rates of nosocomial infections during a 2.5-year period.[87] The incidence of nosocomial MRSA, Pseudomonas and Candida infections per 1000 patient-days were respectively 4.1, 3.9, 38.4 for patients housed in multiple patient ICU rooms and 1.3, 0.7, 13.8 for patients housed in single rooms ($P < 0.001$ for all three comparisons).[87] However, another study conducted in two British ICUs reported that isolating patients had little effect on MRSA acquisition rates.[88]

Screening patients at hospital admission for common pathogens like *S. aureus* may be an effective way to prevent the pathogens from becoming established infections. A recent study estimated the health and economic impacts of preadmission *S. aureus* screening and subsequent decolonisation therapy for the 7.1 million US patients who undergo elective surgery annually. An *S. aureus* screening and decolonisation protocol for all elective surgical patients was projected to save 935 inpatient lives and save $231 million in net medical costs annually.[89]

For some nosocomial infections such as MRSA, 'search and destroy' control strategies have been developed.[90] Such search and destroy protocols involve a number of interventions including: (i) Active surveillance which includes a nasal swab for MRSA cultures upon patient admission and every third day throughout hospitalisation. (ii) Contact precautions including proper gloving, gowning and mask use. (iii) Treatment of carriers with antibiotics and surface disinfectants. (iv) Microbiological controls: starting 48 h after the end of treatment three control samples were taken at colonised sites. If MRSA was isolated, treatment was resumed. (v) Isolation or cohorting: MRSA positive patients were placed in separate rooms or cohorted with other patients with MRSA infection. (vi) Educational programme on infection controls for healthcare workers. Such a search and destroy MRSA programme was found to reduce MRSA infection in a Spanish ICU from 3.5 to 1.7 cases per 1000 patient-days ($P = 0.024$).[90]

The Netherlands has been addressing the MRSA problem since the 1980s with a programme of patient isolation, search and destroy protocols and restrictive antibiotic usage.[91,92] By 2001, MRSA comprised less than 1% of clinical *S. aureus* specimens collected in Netherlands hospitals, while MRSA comprised 28%, 33%, 19% and 50% of clinical *S. aureus* cultures respectively in Belgium, France, Germany and the USA.[92]

Molecular biology techniques such as PCR and gel electrophoresis techniques have been very useful in hospital surveillance and tracking of nosocomial infections.[93] Such techniques can be used to test samples from patients, staff and environmental substrates. Implementation of an enhanced infection control programme which included molecular typing to assess microbial clonality was associated with an 11% reduction of nosocomial infections in a large hospital ($P = 0.027$).[94] This infection control programme was calculated to annually prevent 270 nosocomial infections and save US$2.2 million in net healthcare costs.

Need for adequate nursing staff

Inadequate nurse staffing may increase risk for nosocomial infections.[73] A US study of 15 846 patients in 51 ICU units served by 1095 nurses measured rates of nosocomial infections and nurse staffing levels.[95] ICU units with higher nurse staffing had significantly lower rates of central-line-associated infections, ventilator-associated pneumonia, ducibitus ulcers and 30 day mortality ($P < 0.05$ for all comparsions).[95] A 12-month study from a 1394-bed Taiwanese hospital reported that higher nursing staff levels were associated with significantly lower levels of urinary tract infections

($P < 0.001$), respiratory infections ($P = 0.004$) and pressure ulcers ($P = 0.031$).[96]

Public reporting of HAIs

Public reporting of HAIs may provide a good incentive for hospitals to reduce nosocomial infection rates. In the USA, since 2003, a number of states have passed laws mandating reporting of HAI rates.[97] There is some concern that such reporting of infections may undercount the true nosocomial infection rates.[97] There is also concern about the need for proper adjustment of infection rates for factors such as age, chronic health problems and preadmission health of the patients received by specific hospitals.[97] Many administrative problems have beset these mandating laws. For example, the State of Illinois passed the 'Hospital Report Card Act' (SB 59) in 2003 mandating public reporting of several types of nosocomial infections.[98] However, by January 2008 none of the reporting systems had been implemented.[98]

Preventing urinary tract and urinary catheter infections

About 80—95% of hospital-acquired urinary tract infections originate from urinary catheters.[99] Urinary catheters should be used only if necessary and should be removed as soon as practicable.[99,100] Some studies have indicated that early removal of urinary catheters can reduce urinary tract infection rates by up to 40%.[101] About 15% of urinary HAIs have been linked to improper handwashing and poor aseptic techniques in cleaning the urinary meatus area and inserting and maintaining the urinary catheters.[100] However, studies have shown that vigorous twice-daily meatal cleaning does not seem to reduce urinary infection rates.[100]

Many studies and meta-analyses have reported that silver alloy/silver hydrogel-tipped urinary catheters significantly reduce urinary tract infections. A 1998 meta-analysis of eight published studies reported that use of silver-tipped urinary catheters was associated with a mean 41% reduction of urinary tract infections (95% CI: 0.42—0.84).[102] A more recent study reported that using silver-tipped catheters (both short- and long-term users) was associated with a 57% reduction in urinary tract infections.[103] None of the 50 bacteria and yeasts isolated from these silver-tipped catheters developed any resistance to silver.[103] These studies have also indicated that while silver-tipped urinary catheters cost more than standard catheters, the saving in nosocomial urinary infections far more than pays for the extra cost of the silver-tipped catheters.[102,103] However, according to meta-analysis of urinary catheters inserted for less than 30 days, post-1995 studies have reported that silver-tipped catheters reduce urinary tract infections by a smaller margin than in pre-1995 studies.[104] The reason for this possible reduced effectiveness of silver-tipped catheters after 1995 is not known. The use of nitrofurazone-coated catheters was associated with a 32—98% reduction in urinary tract infections in three recent published studies.[104]

Preventing central venous line and haemodialysis infections

A number of interventions can significantly reduce the morbidity and mortality of central venous catheter (CVC)-related infections.[105] CVCs should be used only when necessary and should be removed as soon as practical, since longer catheterisation periods significantly increase risk for bloodstream infection.[106] Three studies reported that the use of extensive barrier precautions (long-sleeved gown, sterile gloves, mask, cap and large sterile sheet drape) when inserting a central line was associated with a significantly lower rate of bloodstream infections compared with when only gloves and a small drape were used.[107] These studies also found that extensive barrier precautions were very cost-effective in terms of saving costs of nosocomial infections.[108] Other studies have reported that subclavian central venous insertion is associated with significantly lower bloodstream infection rates compared with femoral insertion.[109] Meta-analysis of eight studies reported that use of antiseptic chlorhexidine-containing solutions to prepare the catheter site was associated with a 51% lower risk of catheter-related bloodstream infections compared with when iodine based solutions were used (95% CI: 0.28—0.88).[110]

The institution of multiple interventions at the same time ('bundling') may be the best strategy to reduce CVC-related infections.[105] A huge study of catheter-related bloodstream infections was conducted in 103 ICUs and analysed 375 757 patient-catheter-days.[111] An education programme was conducted in ICUs that included hand washing, using extensive barrier precautions when inserting a CVC, cleaning skin with chlorhexidine, and avoiding the femoral site and the use of unnecessary catheters. Catheter-related bloodstream infections were 7.7/1000 catheter-days at baseline to 1.4/1000 at 16—18 months follow-up (82%

reduction, $P < 0.002$). Another study reported that a multidimensional educational programme for central catheter insertion and maintenance reduced bloodstream infections from 10.8 to 3.7/1000 catheter-days (66% reduction, $P < 0.0001$) and produced a net saving of from $0.2 to 2.8 million in 18 months secondary to reduced bloodstream infection rates.[112]

The use of coated CVCs can also significantly reduce the risk of nosocomial infections.[113] A two-year study at a large Michigan hospital reported that using chlorhexidine/silver sulfadiazene-coated catheters reduced bloodstream infections in hospitalised patients by 35% ($P < 0.0003$).[114] Meta-analyses and many studies have reported that the use of CVCs coated with chlorhexidine/silver sulfadiazene significantly reduces rates of catheter-related infections and significantly lowers hospital costs.[115] Cost savings were estimated to be $196 for each chlorhexidine/silver sulfadiazene-coated catheter used.[116] Use of new agents such as lysostaphin in catheters and catheter lock solutions may also reduce infection.[113] Lysostaphin is an enzyme which effectively breaks up and kills staphylococci in biofilms on catheters.[117]

Haemodialysis patients are at high risk of many nosocomial infections including *S. aureus*, coagulase-negative staphylococci, many types of Gram-negative bacteria and candida.[118] Temporary catheters have the greatest risk of infection and should not be used any longer than necessary. A review of eight studies calculated that mean rates of bacterial infections in haemodialysis patients were about 6.3/1000 days when temporary catheters were used, 2.8/1000 days with cuffed temporary catheters, 0.4/1000 days with polytetrafluoroethylene grafts, and 0.14/1000 days when arteriovenous fistulas are used.[118] Renal patients are at significant risk for hepatitis C (HCV) transmission from haemodialysis procedures. Risk of HCV transmission can be significantly reduced by using separate haemodialysis machines and equipment for HCV^+ and HCV^- patients, proper gloving and other barrier precautions by healthcare workers, proper cleaning of machines and sending all tubing and dialysis units for either disposal or disinfection and reprocessing after each use.[119] A Spanish study reported that HCV^+ prevalence fell from 30.5% (121 patients) in 1993 to 6.8% (161 patients) ($P < 0.05$) in 2003 following the institution of universal precautions and increased cleaning along with the separation of HCV^+ and HCV^- patients. No serconversions were noted during this time in 335 HCV^- haemodialysis patients following separation of HCV^+ and HCV^- haemodialysis.[119]

Preventing ventilator-associated pneumonia

Although prompt use of proper antibiotics is the cornerstone for treating ventilator-associated pneumonia (VAP), there are many non-pharmacological interventions which can significantly reduce risk of VAP incidence. Longstanding methods of reducing risk of VAP include: (i) avoiding tracheal intubation whenever possible and using non-invasive positive pressure ventilation instead; (ii) placing the patient in semi-erect position of 30—45° above horizontal reduces risk of aspiration-related VAP; and (iii) using enteral feeding rather than parenteral feeding whenever possible.[120] Recent meta-analysis has also indicated that the following interventions are associated with significantly lower levels of VAP: (i) kinetic bed therapy (15 studies; RR: 0.38; 95% CI: 0.28—0.53); (ii) subglottic secretion drainage (five studies; RR: 0.51; 95% CI: 0.37—0.71); (iii) heat and moisture exchangers vs heated humidifiers (eight studies; RR: 0.69; 95% CI: 0.51—0.94); (iv) oral decontamination with chlorhexidine (seven studies; RR: 0.74; 95% CI: 0.56—0.96).[121] Five studies employing multiple interventions were able to significantly reduce rates of VAP by 31—57%.[121] One of these studies involved four hospitals and employed an intensive educational programme for ICU nurses and respiratory therapists coupled with posters and fact sheets posted in the ICU.[122] Following these broad based interventions, VAP rates fell from 8.75 to 4.74/1000 ventilator-days (46% reduction, $P < 0.001$).[122]

Control of infections related to surgery and surgical equipment

About 2—5% of all surgical patients develop a significant infection at the wound site.[123] While antibiotics play a major role in preventing and treating surgical infections, many other factors are important in preventing surgical infections. Higher rates of surgical infections are associated with operations of two or more hours, a contaminated or dirty procedure, or inadequate scrubbing procedures.[123] Traditionally patients have been shaved at surgical sites, but it is now believed that clipping hair is better since shaving leaves small cuts in the skin. A review of three trials involving 3193 surgical patients reported that there were significantly more surgical site infections when patients were shaved versus clipped (RR: 2.02; 95% CI: 1.21—3.36).[124] Cleaning surgical sites with antiseptics such as iodine compounds or chlorhexidine has long been recommended to reduce risk of surgical infection. However,

meta-analysis of six studies found that bathing or swabbing sites with 4% chlorhexidine solutions was associated with only a marginal decline in surgical site infection rates compared with bathing with plain soap or placebo solutions (RR: 91%; 95% CI: 0.80–1.04).[125]

Warming the patient before or during surgery has also been shown to significantly reduce rates of surgical infection.[126] Warming may reduce surgical infection rates by improving blood circulation and immune function in the surgical areas. An ultra-clean air-filtered operating room coupled with use of whole-body ventilated exhaust suits by operating personnel was associated with a 60% drop in deep sepsis rates compared with standard operating room procedures ($P < 0.001$).[16]

Multiple interventions simultaneously may prove to be the most effective way to reduce surgical infections. Institution of a comprehensive surgical infection control programme was associated with a 63% drop in surgical-related infections for coronary artery bypass graft patients (OR: 0.37; 95% CI: 0.22–0.63).[127] This infection control programme included prospective surveillance and reporting, chlorhexidine showers, discontinuation of shaving, elimination of ice baths for cardioplegia solution, limitation of operating room traffic, reducing use of flash sterilisation and elimination of postoperative tap-water wound washing for four days.

Laparoscopic surgery should be done instead of open surgery whenever possible, since laparoscopic surgeries generally have significantly lower rates of infection, adhesions and other complications. Many studies and meta-analyses have reported much lower infection rates when laparoscopic surgery is performed instead of open surgery for many types of abdominal procedures including perforated peptic ulcer surgery, cholecystectomy, splenectomy, lysis of small intestine adhesions causing obstruction, appendectomy, rectal cancer surgery and ventral hernia repair.[128–135]

Relatively few studies have been conducted involving sterilisation of surgical instruments and medical devices such as endoscopes. Cleaning must also precede sterilisation or high-level disinfection. Surgical and medical instruments may be sterilised or disinfected by a number of methods including autoclaving, ethylene oxide chambers, or solutions containing phenolics, aldehydes, quaternary ammonium compounds, hydrogen peroxide, peracetic acid or chlorine compounds.[136] All of these techniques have advantages and disadvantages. Autoclaving provides excellent sterilisation but not all equipment can withstand the heat. Ethylene oxide chambers provide excellent disinfection but they must be monitored for potential ethylene oxide gas leaks. Disinfectant aldehydes such as glutaraldehye and *ortho*-phthaladehyde can cause respiratory, skin and eye irritation. Peracetic acid systems provide good sterilisation but are relatively expensive and can only be used for immersible instruments.[136]

Preventing waterborne hospital infections

A number of interventions have been proven effective in reducing rates of hospital waterborne infections. Numerous studies have found that replacing tap water with sterile water for drinking, bathing and procedures can significantly reduce rates of many hospital infections including cryptosporidium, legionella, aeromonas and stenotrophomonas.[22] Sterile sponges can be used for bathing. Boiling and water filtration in hospital water systems can also sterilise water, but these systems need to be monitored closely because many problems can develop which cause these systems to fail.[22] Daily cleaning of patient shower areas with a detergent and phenolic compound has been shown to significantly decrease airborne levels of moulds including aspergillus.[137]

Heating water to more than 50 °C has been shown to significantly reduce levels of *Legionella* spp. in storage tanks and hospital water systems; however, water heating alone will not usually eliminate all legionella in a contaminated hospital water system.[138] Some studies have found that the UV-light water treatment can greatly reduce levels of legionella in hospital water systems.[139] Copper–silver-based ionisation systems can also significantly reduce waterborne concentrations of legionella, moulds and Gram-negative bacteria such as *P. aeruginosa* and *Actinetobacter baumannii*.[140–142] A Spanish hospital saw legionella infection rates fall from 2.45 to 0.18 cases per 1000 discharges following installation of a copper–silver ionisation system ($P < 0.001$).[140] Routine surveillance of hospital water supplies for legionella is highly recommended in cases of confirmed legionella infections; however, it is controversial as to whether such routine testing is needed in hospitals with no legionella infection history.[138,143]

All water leaks and water damage should be repaired and remediated within 24 h to prevent growth of pathogenic bacteria and moulds.[144] Hospitals should avoid using indoor decorative fountains since they encourage legionella and the splashing water facilitates ready aerosolisation of the organism.

Air filtration and air handling

HEPA filtration is relatively inexpensive and probably should be used for all hospital rooms. Various studies have found that the HEPA filtration in hospitals can significantly reduce airborne levels and/or infection rates for several aerosolised pathogens. Many studies have reported that the HEPA filters in patient rooms can significantly reduce both airborne aspergillus concentrations and rates of human aspergillus infections.[145–147] Meta-analysis of six non-randomised controlled trials reported that HEPA filtration for neutropenic patients was associated with a significant drop in mortality due to mould infections (RR: 0.29; 95% CI: 0.15–0.54).[148] Meta-analysis of six randomised controlled studies reported that HEPA filtration for neutropenic patients was associated with only a marginal drop in overall mortality (RR: 0.86; 95% CI: 0.65–1.14).[148]

Use of portable HEPA filters has been found to significantly reduce airborne levels of MRSA and *P. aeruginosa* in hospitals.[149,150] A porcine study reported that HEPA filtration was associated with significantly lower rates of porcine respiratory syndrome virus (PRSV).[151] HEPA air filtration has been shown to reduce airborne concentrations of droplet nuclei (which transport tuberculosis) by 90%.[152]

Recently, a new hospital air filtration system has been developed by Airinspace Technologies (Montigny le Bretonneux, France). This portable Immunair™ system forms a protective hood around the patient, filters air at 60 air changes per hour and uses a 'cold plasma' system to destroy microbes. Early tests have indicated that such a system has a more than 99% single-pass efficiency in destroying bacteria, viruses and moulds such as Aspergillus.[153] More study of this and other air filtration systems is needed.

Provision of adequate outdoor air ventilation rates is also essential to dilute out and control hospital pathogens. A study with army recruits reported significantly higher rates of acute respiratory disease when housed in poorly ventilated barracks compared with well-ventilated barracks.[154] The American Society for Heating, Refrigerating and Air Conditioning Engineers (ASHRAE) has proposed standards of at least four outdoor air changes per hour (ACH) for hospital rooms, 15 outdoor ACH for operating rooms and six outdoor ACH for ICUs.[155,156] Hospitals undergoing construction or renovation have increased dangers for airborne and dustborne pathogens and may require additional outdoor ACH as well as barrier protections.[155,156]

UV light machines in rooms or in ventilation systems can effectively kill mycobacteria, legionella and many viruses, but UV light is not effective in killing many species of bacteria and moulds.[155]

Special interventions for control of tuberculosis

Tuberculosis (TB) remains a serious health problem in both the developed and developing world.[157] Recent CDC guidelines have recommended a number of administrative, engineering and personal protection measures to control TB spread in healthcare settings.[158] Recommended administrative controls include TB testing for all patients at risk of TB, implementing a written TB control plan in the hospital and housing infected patients in separate rooms. All rooms housing TB patients should have at least 12 outdoor ACH, have a negative pressure of at least 0.01 inch water, and the rooms of patients with actual or suspected TB should be checked visually with tests such as smoke tests. HEPA air filters in patient rooms and UV irradiation in the ventilation systems or upper part of rooms is also strongly recommended to reduce airborne TB levels. HEPA masks or other respiratory protection need to be worn by healthcare workers and visitors to rooms of infectious TB patients. Proper cleaning and disinfecting of instruments used by TB patients are also essential.[158]

Controlled studies for individual interventions of TB control programmes are lacking.[157] However, risk of TB transmission can be greatly reduced when many infection control measures are applied simultaneously. A 1000-bed hospital in Atlanta, Georgia, used a variety of controls for TB including administrative (patient isolation, staff TB education programme, TB tests to staff every six months and hiring a nurse epidemiologist), negative-pressure TB rooms, and HEPA masks by all healthcare workers in respiratory protection areas.[159] Over a 28-month period, the number of TB exposure incidents fell from 4.4 to 0.6 per month ($P < 0.001$). The rate of tuberculin skin test conversions among healthcare workers also fell from 3.3% to 1.7% in this period ($P < 0.001$).[159]

Discussion

Many non-pharmacological interventions have been shown to significantly reduce rates of HAIs, but are often overlooked in clinical practice. Widely varied interventions such as proper hand

washing, better nutrition, housing patients in separate rooms, sufficient numbers of nursing staff, coated urinary and CVCs, HEPA air filters, copper—silver water ionisation and numerous interventions for ventilated and surgical patients have all been documented to significantly reduce risk of nosocomial morbidity and/or mortality. Many of these studies have also indicated that these infection control interventions will more than pay for themselves in terms of reduced total medical costs.

The hospital environment is a complicated ecosystem and many interventions are needed for optimal infection control. While many hospitals are using a number of these infection control strategies, relatively few hospitals are employing most of the broad range of infection control methods available today. Multiple interventions ('bundling') often give better results than single interventions.[160] Most bundling studies have used only two to five infection control interventions at the same time.[160] Larger interventional studies should be undertaken which employ large numbers of infection control methods simultaneously. Such multifaceted infection control protocols will probably result in larger declines in nosocomial infection rates than strategies employing only one to five interventions. However, it is difficult to sort out the efficacy of individual interventions when many interventions are simultaneously used. Aboelela *et al*. have suggested that in studies with many interventions, groups of several interventions or bundles can be studied as one intervention.[160]

Current levels of multidrug-resistant bacteria will increase in the future as antibiotics are heavily used in both human and veterinary medicine and relatively few new antibiotics are being developed. Multifactorial non-pharmacological infection control strategies will not only substantially reduce the numbers of nosocomial infections, but should also significantly reduce hospital antibiotic usage. Lower overall antibiotic use will reduce risk of antibiotic-resistant organisms and should improve efficacy of antibiotics given to patients who do acquire nosocomial infections.

Multiple-intervention infection control strategies should significantly reduce mortality, morbidity and overall medical costs. There needs to be more support for improved hospital infection control on the part of patient advocacy groups, nursing, medical and public health associations, hospital administrators, health insurance companies, business and labour groups, the media and public officials. Research and implementation of multifaceted hospital infection control strategies should clearly be one of the highest priority items facing healthcare in the early 21st century.

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