Hospital water point-of-use filtration: A complementary strategy to reduce the risk of nosocomial infection

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Cholera, hepatitis and typhoid are well-recognized water-borne illnesses that take the lives of many every year in areas of uncontrollable flood, but far less attention is afforded to the allegedly safe potable water in affluent nations and the presumed healthful quality of water in communities and hospitals. Recent literature, however, points to increasing awareness of serious clinical sequelae particularly experienced by immunocompromised patients at high risk for disease and death from exposure to water-borne microbes in hospitals. This review reflects the literature indicting hospital water as an important source for nosocomial infections, examines patient populations at greatest risk, uncovers examples of failures in remedial water treatment methods and the reasons for them, and introduces point-of-use water filtration as a practical alternative or complementary component of an infection control strategy that may reduce the risk of nosocomial infections. (Am J Infect Control 2005;33:S1-19.)

Despite advances in health care and with total admissions remaining constant (Figure 1*A*), the rate of hospital-acquired (nosocomial) infections in the United States has actually increased over the 20-year period from 1975 to 1995 (Figure 1*B*).[1]

Successful initiatives to shorten hospital length of stay (LOS) further confound assessment of the true incidence of nosocomial infections, because the incubation period may be longer than the average hospital LOS.[1] Among the types of nosocomial infections, pneumonia is a common cause of morbidity and mortality second only to urinary tract infections in frequency of occurrence and it ranks first among nosocomial infections in critical care settings.[2] The added cost of infectious complications is estimated to range from $15,275[3] to $38,656[4] per infection.

Concern for the health and welfare of the patient should be the most important impetus to control nosocomial infections. Another factor includes cost pressures derived from increasingly scarce professional resources such as critical care physicians and nurses, which drive costs up as well as costly litigation, particularly evident in litigious societies.[5] What proportion of these nosocomial infections may be attributable to hospital water? In a call to arms for physicians and infection control practitioners alike, it has been said that "Although numerous hospital sources cause nosocomial outbreaks, perhaps the most overlooked, important, and controllable source of nosocomial pathogens is hospital water."[6]

LEGIONELLA

An excellent example of the profound implications of water-borne nosocomial infection relate to recent observations of *Legionella*. *Legionella* species *(sp.)* are well recognized as water-borne microorganisms and were made infamous with the devastation of an American Legion Convention in a hotel in Philadelphia in 1976. Since then, its history as a water-borne mediator of morbidity has been reviewed both microbiologically[7] and clinically.[8,9] *Legionella sp.* have been isolated in as few as 1% to as many as 40% of cases of hospital-acquired pneumonia; consequently, underdiagnosis and underreporting are high with only 2-10% of estimated cases believed to be accurately reported.[10]

From the Pall Corporation, East Hills, New York.

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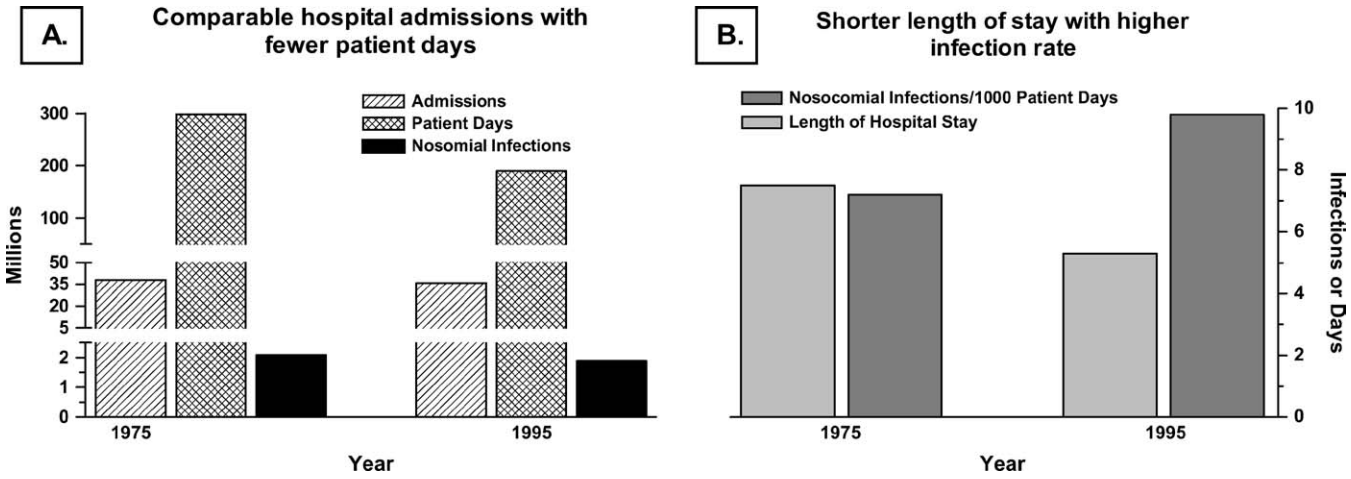

Fig 1. Nosocomial infections are a growing concern in US hospitals (adapted from Weinstein[1]) (see also http://www.cdc.gov/ncidod/eid/vol4no3/contents.htm).

Transmission of *Legionella sp.* from hospital water can occur by inhalation of aerosolized microbes that are commonly generated during showering[11] or running bath water.[12] Equipment washed or rinsed with contaminated water can also confer infection.[13]

Hospital water supplies are frequently contaminated with *Legionella sp.*[14-16] and recent evidence of nosocomial infection is also available[17] making this microorganism one of current concern. In one study, 55% of transplant units in the United Kingdom tested positive for *Legionella*[18] as well as 80% of 11 hospitals sampled in Italy.[19] A hospital in Canada reported nearly 25% of the 2200 samples taken over 4 years were positive for *Legionella* with some locations more problematic than others.[20]

Interestingly, guidelines for the prevention of health-care-associated pneumonia include the routine culturing of water systems for *Legionella sp.* limited, however, to patient-care areas at high risk for infection.[21] Despite this observation and with many regulations in place to support prevention and detection, a recent survey shows that ''…only 5% of health care facilities have developed and implemented a waterborne pathogen risk management plan for building water systems.''[22] This underscores the perception by many that *Legionella sp.*, and to a greater extent other microbes, are not recognized for the dangers they present.

OTHER BACTERIA

Three major categories of water-borne nosocomial infectious organisms, including bacteria, mycobacterium and fungi have been delineated and are shown in Table 1 modified from Anaissie and co-workers.[6] Many of these organisms were shown to be resistant to antibiotics.[6] Additional evidence was compiled by the authors suggestive of a causal relationship between contaminated hospital water and infectious complications. The causal relationship is supported by the use of antibiograms, serotyping or temporal association and supports the view that nosocomial infections may be derived from hospital water-borne microorganisms such as *Campylobacter*,[23] *Aeromonas*,[24] *Flavobacterium*, *Enterobacter*, *Serratia* and *Klebsiella sp.* Other literature reviews support these observations.[25,26] Adding to the compendium is a recent report of a *Mycobacterium simiae* outbreak from contaminated hospital water[27] and *Mycobacterium* is frequently recovered from hospital water.[28]

Pseudomonas is an organism that can cause serious nosocomial infection.[29] Stamm-Balderjahn[30] and coworkers, presenting at the Society for Healthcare in Epidemiology (SHEA) meeting in April 2004, reviewed the literature disclosing Pseudomonads as one of the most frequently reported pathogens concerning nosocomial outbreaks. The results (expressed as percent of total) are shown in Figure 2 and illustrate blood stream infections occurred most often and the most frequent environmental source reportedly is hospital water.

The timeliness and increasing awareness of the dangers of hospital water are reflected in the observations of clinicians at a hospital in Lebanon citing ''…potentially the largest single-source nosocomial bloodstream infection outbreak ever reported, and the first report of an alcohol skin antiseptic contaminated by tap water as a source for nosocomial bacteremia.''[31] Moreover, the contribution of tap water and environmental surfaces towards bronchoscope and endoscope mediated transmission of antibiotic-resistant

Table 1. Evidence correlating infection inpatients with microorganisms found in hospital water

Organism	Site of infection	Molecular-relatedness evidence	Number of reports
Bacteria			
Pseudomonas aeruginosa	Blood, CVC, lungs, peritoneum, sinuses, trachea, urine	PCR; DNA macrorestriction analysis, PFGE, ERIC-PCR, RAPD, DNA fingerprinting, DNA typing, serotyping, phage typing, serogrouping, genotyping, ExoA DNA probe, biotyping, electrophoretic esterase typing	10
Stenotrophomonas maltophilia	Blood, peritoneum, respiratory tract, skin, stools, throat, trachea, urine	PFGE, RAPD	4
Serratia marcescens	Eye, stools	PFGE	1
Acinetobacter baumannii	Skin, wound	PFGE, biotyping	1
Aeromonas hydrophila	Blood	electrophoretic esterase typing	1
Chryseobacterium species	Blood	AP-PCR	1
Mycobacterium			
Mycobacterium avium	Disseminated	PFGE	1
Mycobacterium fortuitum	Disseminated, respiratory tract, sputum, sternal wound infection wound	AP-PCR, PFGE, phenotype analysis, plasmid profiles,	4
Mycobacterium xenopi	Various, spine	PCR-based techniques, chromosomal restriction fragment patterns	2
Mycobacterium kansasii	Abscess, blood, bone, sputum, stomach, urine	RFLP, PFGE	1
Mycobacterium chelonae	Sternal wound infection, prosthetic valve	Electrophoresis of enzymes, plasmid profiling	1
Fungi			
Fusarium solani	Disseminated	RFLP, RAPD, IR-PCR	1
Exophiala jeanselmaei	Disseminated	RAPD	1
Aspergillus fumigatus	Lungs	PCR, SSPD	1

Adapted from Anaissie et al.[6]
CVC, central venous catheter; *AP*, arbitrarily primed; *PCR*, polymerase chain reaction; *PFGE*, pulse-field gel electrophoresis; *ERIC*, enterobacterial repetitive intergenic consensus sequencing; *RAPD*, random amplified polymorphic DNA; *ExoA*, exotoxin A; *RFLP*, restriction fragment-length polymorphism; *AFLP*, amplified fragment-length polymorphism; *IR*, interrepeat; *SSPD*, sequence-specific DNA primer analysis.

nosocomial *Pseudomonas aeruginosa* infections was reviewed recently, and a compelling argument for their role as a contributing factor in clinically important disease was provided.[32]

MOLDS

Fungi including molds and yeasts were cultured from hospital water and their reported prevalence was quite high[33] and observed by others.[34,35] Among 126 potable water samples, two-thirds of which came from hospitals, molds were present in nearly 83% and yeasts from 11%. *Aspergillus* was recovered from 53, or a third, of the samples. Interestingly, a pattern emerged showing yeasts were correlated with coliforms, whereas filamentous fungi correlated more with total heterotrophic bacteria counts. Therefore, detection of elevated heterotrophic plate count might be a prognosticator of filamentous fungal infections.

Aspergillus species abound in the hospital setting and the rise in prevalence has startled some.[36] Molecular biology techniques applied to water and air-borne

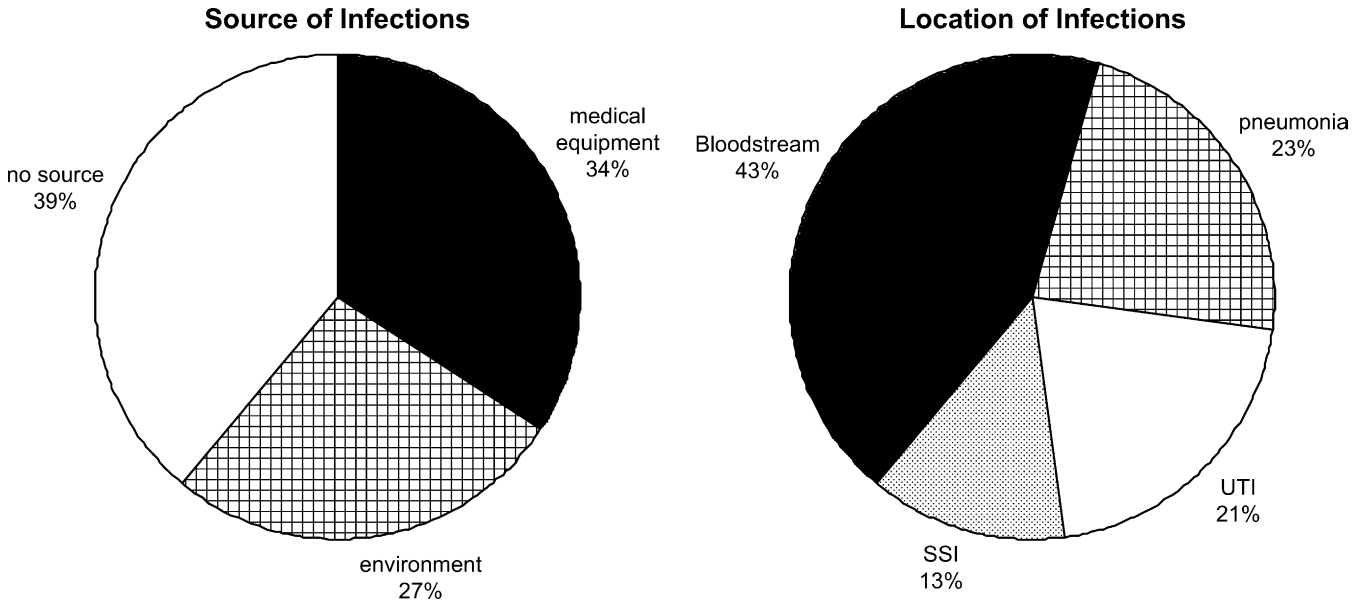

Fig 2. Distribution of *Pseudomonas* nosocomial infections reported from 91 outbreaks over the period 1965-early 2004 (adapted from Stamm-Balderjahn et al[30]). Abbreviations: UTI, urinary tract infections; SSI, surgical site infections.

Aspergillus confirm these as the source of infections in patients.[37] Recent studies were performed in a hematologic malignancy patient population immunocompromised by virtue of their disease or the chemotherapy treatment they require. Molds, including *Aspergillus*, were recovered from 70% of water samples, 22% of swabs from the plumbing and 83% of indoor air in over 1900 samples taken in a bone marrow transplant unit. Results of the study strongly suggest that the mold recovered from indoor air derives from aerosolization of the shower water.[38] These data support previously espoused views suggesting that re-aerosolization of mold from shower walls can occur and serve as a mechanism of infectivity.[39]

VIRUSES

A number of viruses are known to be transmitted through water and most notable among them are rotavirus, para-rotavirus, reovirus (reoviridae), hepatitis A and E, and norovirus (formerly known as the Norwalk virus).[40] Water-borne hospital acquired viral infections are documented as well.[41,42] However, since they cannot proliferate outside of a host, their numbers tend to be naturally lower than other microbes.

PROTOZOA

Community-acquired water-borne infections are well known, and caused by the protozoans, *Cryptosporidium* and *Giardia* where the former was popularized by an outbreak in Milwaukee, Wisconsin, in 1993 affecting over 400 thousand citizens.[43,44] The fact that these organisms can pass through treated water that meets quality standards suggests that these standards may be inadequate[45] and *Cryptosporidium* as a contributor to nosocomial infection is gaining increasing attention.[25,46] Not surprisingly, there are data demonstrating nosocomial infections from *Cryptosporidium parvum*[47] as well as *Giardia intestinalis*.[48]

Protozoa can contribute to nosocomial bacterial infections. Some protozoa can serve to protect bacteria from the biocidal effects of sanitation treatment methods.[49,50] Protozoa, like those of the *Acanthamoeba* species, feed on bacteria. However, some bacteria can resist the digestive actions of their host and either destroy it or enjoy a symbiotic relationship providing it safe passage to an environment free of microbicidal activity. Organisms known to be involved in such mechanisms include …''*Cryptococcus neoformans*, *Legionella sp.*, *Chlamydophila pneumoniae*, *Mycobacterium avium*, *Listeria monocytogenes*, *Pseudomonas aeruginosa*, and *Francisella tularensis*, and emerging pathogens, such as *Bosea spp.*, *Simkania negevensis*, *Parachlamydia acanthamoebae*, and *Legionella*-like amoebal pathogens.''[49]

Therefore, a variety of microorganisms can be found in hospital water and are shown to have caused morbidity in patients. Some patients are at greater risk than others.

PATIENTS AT RISK

Patients who are immune compromised appear most susceptible to the risks of infectious complications

consequent to exposure to contaminated water sources, an observation that has been substantiated by a number of recent reviews.[26,51-53] Included in the high-risk category are intensive care ward patients,[15,54-58] neonates[59-65] and patients with HIV and AIDS,[66-69] cystic fibrosis,[70] those undergoing renal dialysis,[71] transplantation,[72-75] hematologic procedures,[76-80] cancer therapy,[81] and burn treatment.[82-86]

Immune status is not the only predictor of susceptibility to infectious complications as summarized in a model described by Duncan and Edberg[87] (Figure 3). Microbe virulence, dose of exposure and immunological status of the patient or target organ all contribute to the risk of disease development. Dose and/or virulence of microbial exposure may be a factor that contributes to certain water transmitted infectious complications documented subsequent to surgical,[88-90] or moderately invasive diagnostic procedures such as endoscopy,[13,32,91-93] laparoscopy[94] or colonoscopy,[95] where the patients are considered relatively immune competent. Alternatively, the gut manages a complex immune response to the myriad challenges presented to it and if altered by physical trauma or disease, infection can occur through this route.

It is important to appreciate the source of contaminated water reaching the patient. The sources of water-borne microbial contamination that have been identified as causative in transmitting disease are numerous and include hospital water,[54,58,62,90] plumbing fixtures, faucets and sinks,[61] bathtub,[59] showers and shower heads,[11,96] humidifiers,[88] ice machines,[97-101] hydrotherapy equipment,[83,86] pharmacy deionized water,[102] tap water aerators,[81] bath toys[64] and hemodialysis fluid.[103] All may derive, of course, from a common source of tap water.

RELATIVE RISK

The foregoing discussion illustrates the varied patient population in whom nosocomial infection derived from water-borne organisms present. Not all patients fall into the classification of those presumed or confirmed to be immune compromised. Moreover the notion of immune competency is more a function of the immune status of the target organ, number of microbes (classic dose-response relationship) and the virulence of the microorganism. This is particular true for water-borne organisms leading to gastritis and enteritis.[87]

However, it is intuitively attractive to view generally immunocompromised patients as being at greater risk for any infection compared with those who are immune competent, and this has been well-detailed in a recent review.[53] The authors summarize the risk for infection based upon the level of immune competency, infectious dose, virulence of the organism and predilection of the pathogen for a target organ or tissue. From a practical perspective, they emphasize their previously published[104] categorization of patients with different degrees of immune suppression and suggested corresponding levels of protection against contaminated drinking water. An adaptation of their schema is shown in Table 2, modified by including additional patient groups derived from the discussion above. These patients are suspected to be immunocompromised to some extent.

$$\text{Infection} \propto \frac{[\text{Number of Microbes}] \times [\text{Virulence Characteristics}]}{\text{Immune Status of the Host}}$$

Fig 3. Relationship reflecting the risk of acquiring a nosocomial infection.[87]

It is worth noting that we included transfusion recipients in the mildly immunocompromised group although consensus is lacking. However, the controversy over the clinical implications of the immunosuppressive effect of transfusion has been reviewed and there are ample data to support the view that transfusion recipients are immune compromised.[105,106]

Preventing water-borne nosocomial infections can be approached by controlling that which is amenable to control. Immune competency of the patient may be out of reach during the course of treatment. Virulence of the microorganism is biologically determined and can be altered by changing the environmental conditions with the presence of antibiotics, pH altering agents and perhaps even iron chelators. The dose of microbes, however, is the easiest to address and should be the first target in preventing or minimizing water-borne nosocomial infections and we look to standards for guidance in how to accomplish this.

RISK MANAGEMENT WITH STANDARDS

Unfortunately, there are no international drinking water standards. The World Health Organization (WHO) publishes the Guidelines for Drinking Water Quality,[107] which many countries use as the basis to establish their own national standards for community water. Guidelines are what the name implies, recommendations that are without legal implication but ''standards'' have regulatory significance and are enforceable. The guidelines represent a scientific assessment of the risks to health from biological and chemical constituents of drinking water and of the effectiveness of relevant control and treatment measures.

Table 2. Characterization of patient populations at risk for infection from drinking water and corresponding risk-risk reduction behaviors

Immunosuppression level	Patient population	Risk reduction behavior
None	Minor surgical or diagnostic procedures (endoscopy, laproscopy, colonscopy)	No exposure of medical devices to tap water
1. Mild	Acute or chronic leukemia, malignant lymphoma, childhood histiocytosis X under maintenance without neutropenia	Avoid any circumstances with elevated infection risks (such as drinking water from uncontrolled sources)
	Solid tumors (within 6 mo of chemotherapy)	
	Long-term corticosteroid therapy with <20 mg/d prednisone or equivalent	
	Autologous stem cell transplant (within 6 mo of discharge)	
	Surgical patients.	
	Blood component transfusion recipient	
	Cystic fibrosis	
	Renal dialysis	
2. Moderate	Acute or chronic leukemia, malignant lymphoma, childhood histiocytosis X solid tumors under intensive treatment (expected duration of neutropenia <500/μL for ≤10 days)	Drinking water should have an additional antimicrobial barrier to tap water
	Long-term corticosteroid therapy with ≥20 mg/d prednisone or equivalent	Bathroom installations should be controlled for bacterial reservoirs
	Solid organ transplant after intensive treatment phase	
	AIDS with a count of CD4+ cells less than 200 μL	
	Burns: Second-degree burns covering 15% to 20% of the body on an adult or covering over 10% to 20% of the body on a child	
3. Severe	Acute or chronic leukemia, malignant lymphoma, childhood histiocytosis X solid tumors under intensive treatment (expected duration of neutropenia <500/μL for >10 days)	Any water for human use should have a very low bacterial count (use water filters/ controlled carbonated water)
	Solid organ transplant under intensive treatment phase (induction or rejection therapy)	Strict control of bath installation and water for showering (showering to be avoided if no control possible)
	Allogeneic stem cell transplant (first 6-12 mo after engraftment)	
	AIDS with a count of CD4+ cells less than 200 μL and an additional factor of immunosuppression (eg, neutropenia, corticosteroids)	
	Second-degree burns covering more than 20% of the body.	
	Third-degree burns covering more than 10% of the body	
	Any fourth-degree burn.	
	Neonates	
4. Extreme	Allogeneic stem cell transplantation (until engraftment)	Only sterile fluids for drinking, mouth care, and washing allowed

Adapted from Glasmacher et al[53] and Engelhart et al.[104]

At the current time it is difficult to find a compilation of guidelines and regulations encompassing a global view of microbial contaminants in drinking water. The US FDA has enacted legislation that addresses this topic in an indirect way.[108] If total heterotrophic plate count (includes all bacteria) exceeds 500 CFU/mL then attention is directed toward the water treatment method. Coliforms must not be detected in more than 5% of samples processed with a minimum of 40 samples per month. Fewer than 40 per month reduces the limit of tolerance to no more than 1 coliform positive sample. It is suggested that the treatment be adjusted to result in levels of bacteria below this value. It is implied that *Cryptosporidium* and *Giardia* will be addressed if the treatment method is adequately adjusted.

There are minor differences throughout the global community but common to all is a focus on coliform

bacteria. Canada has established similar limits of <500 CFU/mL total heterotrophic plate counts and zero coliforms in a 100 mL sample.[109] The UK,[110] Italy,[111] Germany,[112] Belgium,[113] and New Zealand[114] use the zero coliform in 100 mL sample rule with no attention afforded to other microorganisms.

RISK MANAGEMENT IN THE HOSPITAL

In hospital or health care settings, nosocomial infection is a concern, and hospital water may be a source of patient exposure. What is the approach to guidelines or standards for hospital water? Table 3 shows a contrast between the US Centers for Disease Control (CDC) guidelines, Germany's ordinance and France's guidelines where it addresses high-risk patients exposure to *Legionella* in hospital water. The Table shows the European community at least beginning to acknowledge, identify and make recommendations for high-risk patients within the hospital. There is heterogeneity with approaches for monitoring and reporting hospital-borne pathogens.

However, attesting to the increased concern over nosocomial infections, the Joint Commission on Accreditation of Healthcare Organization (JCAHO pronounced ''jayco'') is implementing a requirement to report hospital acquired infections (HAI) with a phase-in beginning January, 2005 before full enactment in July.[115] These data will provide an opportunity to enhance our understanding of the magnitude of the contribution of contaminated hospital water to nosocomial infections. Water should be considered one unprotected source of exposure to be investigated. There are good reasons why hospital water has been above suspicion as a source of nosocomial infections.

CONTAMINATION CAN BE UNDERESTIMATED

Although most guidelines and standards feature coliforms as the foremost marker of microbial water quality, there are clearly opportunities for contamination to be missed and this can lead to clinical morbidity. These opportunities are availed through:

- plumbing and water flow considerations with the elaboration of a microbial-derived microenvironment of self-protection in the form of ''biofilm'' and,
- underestimates of the true bioburden associated with variations in test methodologies intended to quantify the microbial bioburden.

BIOFILM

In aqueous environments, microorganisms preferentially colonize surfaces to increase their chances of survival.[116] To aid their adhesion to surfaces, copious amounts of sticky extracellular polysaccharides (EPS) are produced which ultimately envelop the cells. Water channels or void spaces of variable size are dispersed throughout the EPS and microbial cell complex, allowing nutrients to diffuse in, and waste products from cell metabolism to be removed out of the gel-like network.[117] A biofilm may therefore be defined as ''an organized community of both viable and non-viable microorganisms, EPS, absorbed nutrients and entrained particles adherent to an inert or living surface.''[118] Microbial cells account for only a small percentage of the volume in biofilms (5-25%), with the polymer network (which contains 70-90% water) occupying the remaining volume.[119-121] Although many different microbial species can form biofilms, the mechanisms involved in biofilm formation are generally similar in each case.[122,123] This process is summarized for water-borne bacteria colonizing any environmental surface and further explained with the assistance of Figure 4.

Briefly, surfaces are rendered attractive to microbes with a pre-conditioning coat such as protein.[124] Bacteria are transported to a pre-conditioned surface by a combination of Brownian motion, frictional drag, electrostatic attraction, gravitational forces and turbulent ''downsweeps.''[125,126] The cells reversibly attach to the surface, followed by an irreversible stage when EPS is produced in large quantities. Cell proliferation occurs, resulting in a monolayer of cells which ultimately results in the formation of microcolonies within an EPS matrix i.e., a biofilm. A typical example of biofilm is shown in Figure 5 in contrast with similar surface not exposed to bacteria.

Cell growth in the biofilm continues until a critical size is reached. Recently, the importance of intercellular communication between bacterial cells, a phenomenon also known as quorum sensing on biofilm formation has been realized.[127-130] During the initial stages of biofilm formation, bacterial cells adsorb to the surface and release signals, known as autoinducers, into the surrounding environment. Autoinducers attract other bacteria to the surface, and induce cell division of adsorbed cells. The intracellular communication continues until the population reaches a threshold level at which the biofilm can be sustained.[131]

Further surface colonization may occur if sections of biofilm are forcibly removed by shear forces operating on the biofilm (erosion or sloughing), or by the controlled release of single, daughter cells from the outer perimeter of the biofilm. Although not fully understood, the latter is believed to be genetically controlled,[132] and as such, cannot be easily controlled by existing water quality maintenance programs. Other factors can contribute to biofilm formation and are summarized in Table 4. This means that any area of the

Table 3. Global potable water quality guidelines and standards

	USA-CDC guidelines[21]	Germany ordinance[183] (operative as of January 2003)	France guidelines[184]
Identified organisms concerned	*Legionella* species	Addresses proliferation of pathogens as: *Legionella species*, *Pseudomonas aeruginosa*, *Acinetobacter*, and others that are bound to biofilms	*Legionella pneumophila*
Environmental surveillance	No recommendation can be made about routinely culturing water systems in health care facilities that do not have patient care areas (eg, transplant units) for persons at high risk for *Legionella* infection	Local public health authorities play role in inspection, supervision of water installations, surveillance, and risk assessments	Routine sampling in hospital area for high-risk patients (immune compromised, transplant, NICU, corticotherapy patients) to assure that *L pneumophila* concentration is below level of detection.
	Periodic culturing for Legionellae in water samples from the transplant unit(s).	Addresses all hospital departments	Sampling points and size recommended
Routine treatment for water quality	Where practical, maintain potable water at the outlet at >51°C (>124°F) or <20°C (<68°F), especially in facilities housing organ transplants or other patients at high risk	Recognizes biofilms and that they are less affected by disinfectants	Create safe points of use for water for high-risk patients where specific water treatment methods are employed
		Compared with pathogens within house plumbing, systems are not allowed at levels that have adverse effects on human health, eg, concentrations <1 CFU/mL[112]	The aim of preventative actions is to eliminate conditions favorable to the survival and proliferation of *Legionella* and limit their distribution in aerosol form. Point of interest is not only the tap but showers and hand sprays.
Disinfection-specific after outbreak	If heated water system is implicated, decontaminate by superheating (71°C-77°C) flushing system minimum of 5 minutes or by hyperchlorination	Changing the prevention strategies and indicate that point-of-use filters on water taps and fittings in intensive care units have led to a distinct reduction of rate of infections	Treatment option is 0.2-μm filtration.
		Advantage of filtration is also cost cutting potential of antibiotic use	Continuous use of disinfectants in hot water is to be avoided
		For high-risk areas of hematology-oncology wards and intensive care units, point-of use filter systems are now recommended	
Reporting requirements	Contact the local or state health department or CDC if the disease is reportable in the state or if assistance is needed	Every irregularity detected must be reported to the local public health authority	Requirements to report to public health authority and National Reference for *Legionella*

water distribution both leading to and within the hospital environment may be subject to biofilm formation as indicated in Figure 6 and further explained in the legend.

RESISTANCE OF BIOFILMS

Surface-associated microorganisms greatly outnumber planktonic cells, and research has shown that biofilm bacteria (sessile bacteria) are profoundly different from planktonic cells (free-living bacteria), and demonstrate some unique characteristics not observed if the cells are returned to the planktonic state.[125,132-135]

It has been widely reported that biofilm bacteria have an increased resistance to antimicrobial agents, compared to their planktonic counterparts. The application of increasingly sophisticated technologies for studying biofilms, including confocal scanning laser microscopy (CSLM) and molecular fluorescent probes have helped to elucidate some potential factors involved in this resistance. However, it seems likely that a combination of factors contributes to this phenomenon:

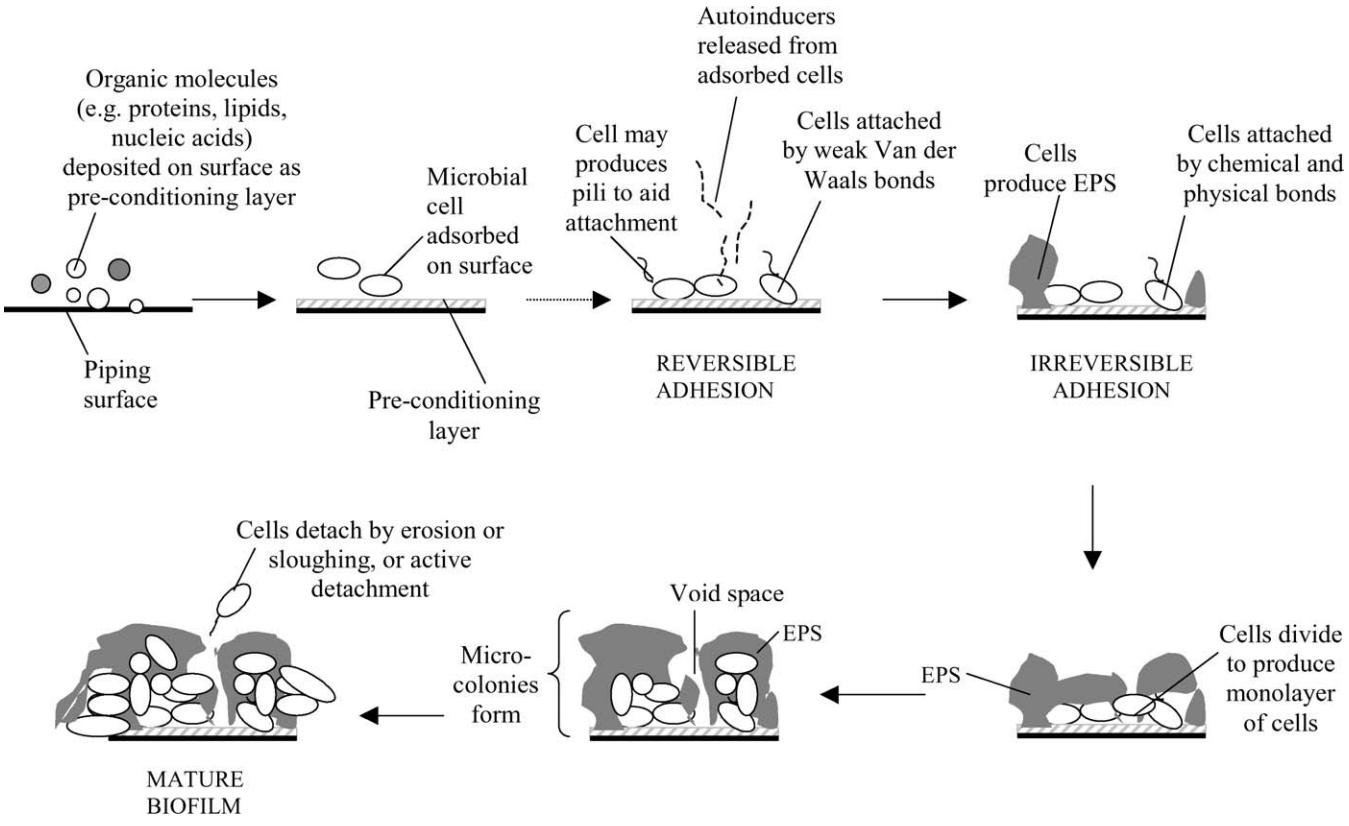

Fig 4. Biofilm formation adapted from several references.[122,126,204-207]

- The antimicrobial agents may fail to penetrate through the thick EPS, the dense cell aggregates and microcolonies, or bind to the polymeric matrix before they reached the target cells.[116,136,137]
- The chemicals may not be effective over the range of cell growth rates and microenvironments distributed through the biofilm (e.g. facultative anaerobes growing in center of biofilm).[138-141]
- Resistance of bacterial cells may be increased by genetic transfer within cells in close proximity in the biofilm.[142,143]

REMOVAL OF BIOFILM

Adequate management of hospital water systems is a key factor in microbial control, and various physical and chemical approaches are employed (Table 4). Chlorination is undoubtedly the most commonly used treatment, though it has been demonstrated that monochloramine is more effective on biofilms.[144,145] Other chemical treatments include the application of silver or copper ions, which have been shown to be effective against *L. pneumophila*.[146] Ozonation may also be considered for microbial control in water systems, though the short half-life, potential incomplete penetration of biofilm and cost associated with treatment makes this a less commonly employed mechanism.

Physical treatments include the application of heat, ultraviolet irradiation and filtration The use of heat must be carefully considered, as research has shown that water held in a storage tank at 30-54°C may induce the proliferation of *L. pneumophila* and thermophilic non-tuberculosis *Mycobacterium* (NTM) *sp*., both of which are capable of growth in temperatures up to 45°C.[25,147] There is also evidence that bacteria may become resistant to UV irradiation at 254 nm (the wavelength used for microbial control), and that exposure time may be inadequate to ensure all microorganisms present in the water are treated.[148-151]

QUANTIFICATION OF WATER-BORNE BACTERIA

In the face of voluminous medical literature it is difficult to envision how hospital water contamination has escaped attention as an important source of microbial exposure to patients. Biofilm has likely played an important role in perpetuating the mystery and so too have methods of testing for water-borne organisms.

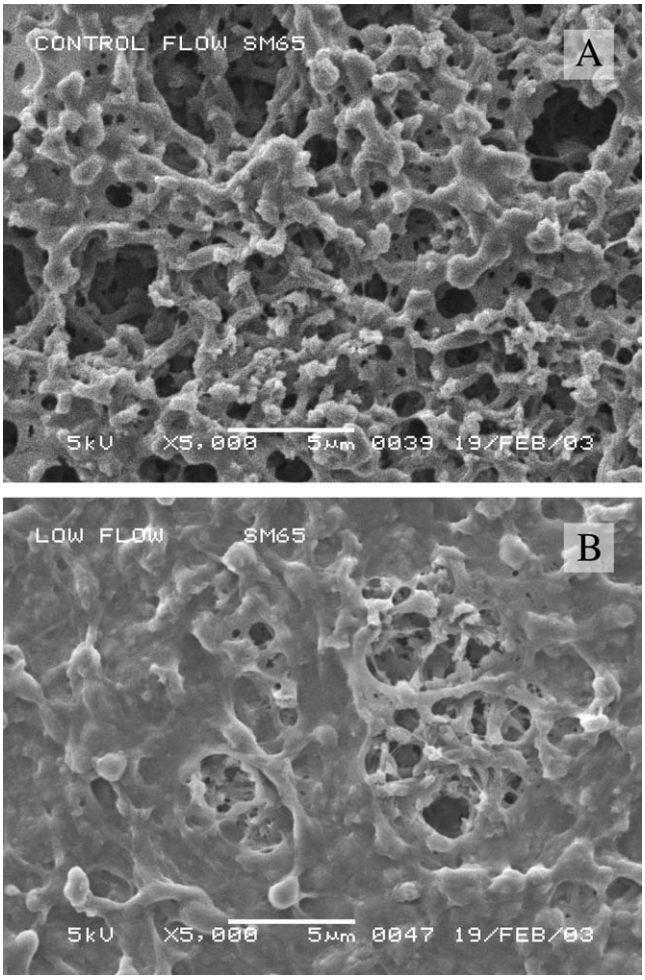

Fig 5. Electronmicrograph of 0.2-µm nylon (Posidyne) filter media subjected to sterile saline (panel A) vs. *P. aeruginosa* suspension (1×10^5) CFU/mL (panel B) for 1 hour daily for 7 consecutive days at low flow (10 mL/min).

Table 4. Some factors affecting biofilm formation in water systems

Factor	Influence on biofilms	Reference numbers
Water chemistry	Multivalent cations (Ca^{2+}, Mg^{2+}) stabilize EPS network Assimilable organic carbon (AOC) levels >50 µg/L may be conducive to microbial growth	185-187
Flow	Influences biofilm structure Laminar flow forms circular microcolonies Turbulent flow forms filamentous-like microcolonies	188
Water stagnation	Dead-legs, heat exchangers, and holding tanks create suitable environment for bacterial colonization and proliferation	150, 171, 189
Piping materials	Smoother, inert surface in piping minimizes biofilm formation and allows improved contact with disinfectants	190
Piping corrosion	Efficiency of chlorination on biofilm removal lowered Production of corrosion products (eg, phosphates, carbonates) may provide nutrients to biofilm	191
High shear stress	Increased resistance to detachment but increased time required for cell attachment	192
Regular flushing of piping	Increased removal of planktonic organisms	187

It should be appreciated that water-borne organisms grow in nutrient-poor environments and have to adapt to nutrient-rich physiologic fluids. While most hospitals routinely sample their water sources for bioburden content, the methods employed vary considerably, and may lead to potential underestimation of the true extent of contamination. It is imperative to realize that bacteria residing in water are fundamentally different than those surviving in a nutrient-rich environment.[152,153] Due to the low nutrient content of drinking water, bacteria surviving in such environments, referred to as oligotrophic bacteria,[154] have evolved several ways to survive, including a broad substrate range, growth at low nutrient levels (1-15 mg carbon/L), lower metabolism rates, a decrease in cell size, and increased cell surface area and adhesion to surfaces.[153,155-158] The methods used to quantify water-borne organisms should involve the use of nutrient-poor growth media, such as R2A. Whereas, attempt to grow water-borne organisms in nutrient-rich media, such as heterotrophic plate count agar (HPCA), will underestimate the bioburden.

Therefore, when using plate culture methods to determine the bacterial content of water, use of a dilute growth medium such as R2A media[159] is generally favored, and significantly higher bacterial recoveries have been reported with dilute medium as compared with recovery on high nutrient growth media e.g. HPCA.[154,159-161] Similarly, plates should be incubated at 25-30°C for a minimum of 7 days to maximize bacterial recovery.[159,160,162-164] To emphasize the point, we have undertaken a comparison of HPCA and R2A media by inoculating plates with each of the two media using an aliquot of the same water sample and incubated the plates at 25°C for up to 15 days. The

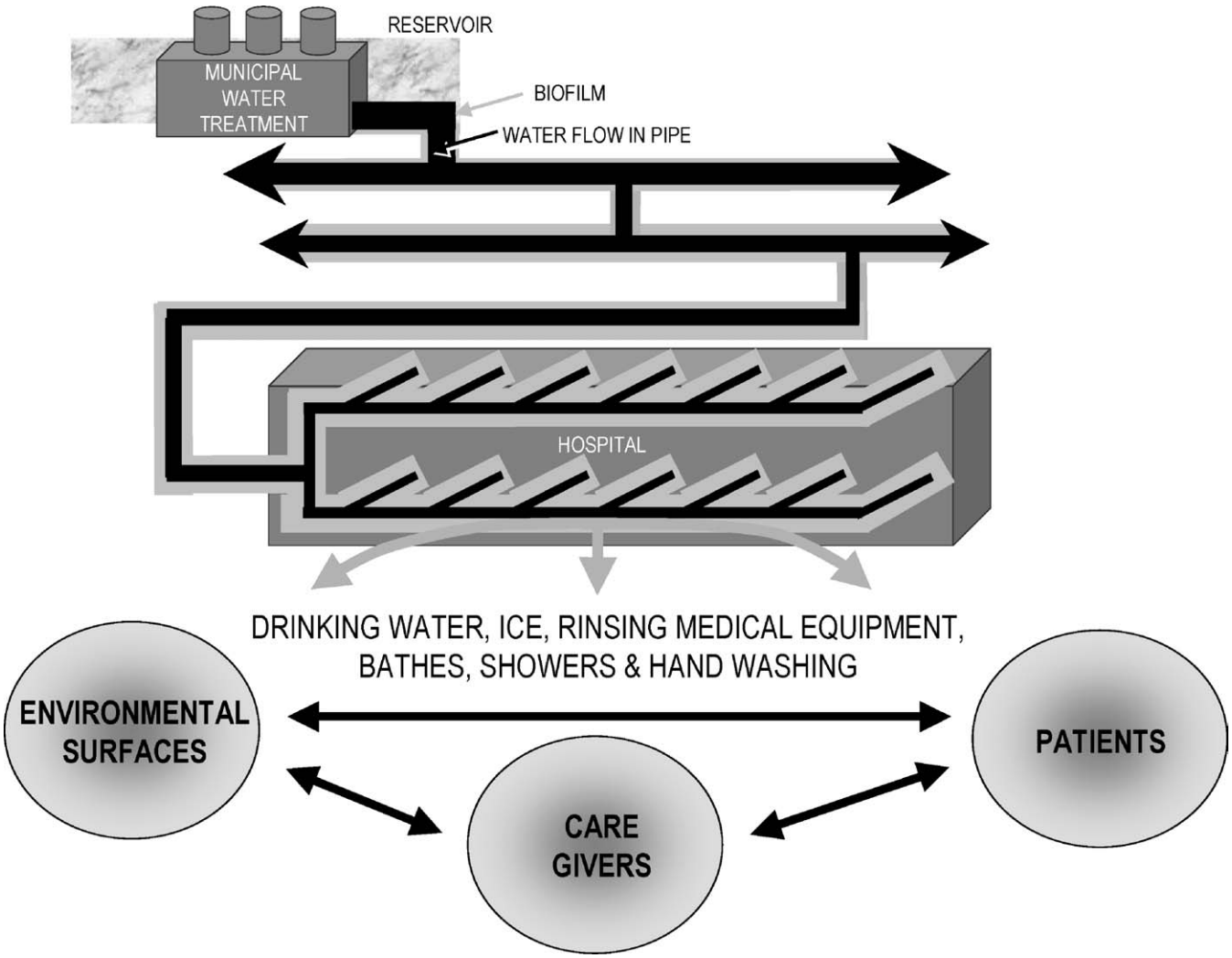

Fig 6. Pictorial representation of the mechanisms by which contaminated hospital water may contribute to nosocomial infections (adapted from Anaissie et al[6]). Flow diagram depicting the accumulation of biofilm from water treatment facility to its point-of-use in the hospital. Large pipes bear high flows at a location very close to the source of treatments to limit the bioburden of microorganisms. As the distribution of water is divided into smaller and smaller pipes with more variable flow with changing patterns of use, biofilm can elaborate to considerably greater extents. At the point-of-use, biofilm can serve as a repository for the continual presentation of viable microbes to patients, care givers, and environmental surfaces with which water may come in contact.

data, shown in Figure 7, illustrate the growth of microbes in R2A far exceed levels obtained from HPCA.

Other methods are available for bacterial detection, including ATP quantification,[165] epifluorescence microscopy,[166] and molecular based methods, such as polymerase chain reaction (PCR) gene probes[151,167] and 16S rRNA sequencing.[168] However, these methods tend to be more costly, require specialized equipment, and trained operators to ensure correct sample preparation and data interpretation.

There are now sufficient data to support the view that pathogens contaminate hospital water, biofilm compromises the efficacy of common treatment methods, standards are not optimal and testing may underestimate the true level of contamination. A simple solution to minimize the bioburden presented to patients may be a physical barrier in the form of point-of-use filtration for faucets and shower heads.

THE SIMPLICITY OF FILTRATION

Although 0.45 micron (μm) filtration was the standard filter grade designed to prevent the passage of bacteria, it is generally accepted that 0.2 μm filters represent a more effective barrier to bacteria transmission.[169] Although rare, there are conditions under

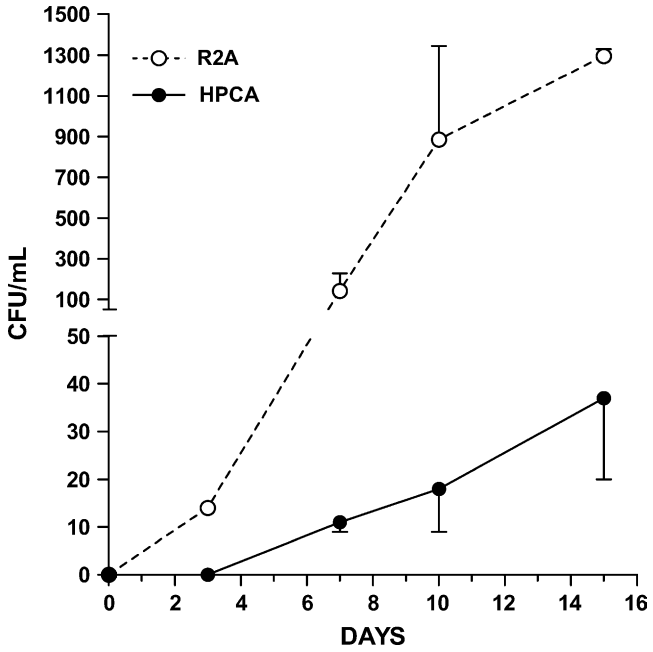

Fig 7. Effect of media composition on growth and quantification of waterborne bacteria from tap water samples. Tap water samples (n=3) were recovered from a domicile in a relatively affluent suburban community just outside of metropolitan New York. Equal volume aliquots were serially diluted in distilled deionized water and 100 μL were plated onto R2A or HPCA, incubated at 25°C and counted following days of incubation indicated.

which water-borne microbes can be recovered in the filtrate of such sized filters and some have argued 0.1 μm confers more absolute performance.[170] The CDC [United States Centers for Disease Control] has identified, as an alternative to sterile water, 0.2 um filtered water to meet the standard of the highest quality of water that is practical for final rinse of endoscopes and other medical devices.[21,171]

In the context of hospital water filtration, 0.2 μm filters are being used with success. In a pediatric nephrology unit with a case of Legionellosis, a look back investigation revealed 5 cases. *Legionella pneumophila* serotype 6 was identified in hospital water limited to the unit and clinicians elected to implement point-of-use water filtration as part of their infection control strategy since the outbreak was restricted to their unit and the installation and maintenance of filters were cost permissive.[11]

At the 9th European Congress of Clinical Microbiology and Infectious Diseases held in Berlin in March, 1999, Hummel and co-workers,[172] used point-of-use water filters. Filters were employed as part of an infection control strategy to minimize exposure to *Legionella* serogroup 1 in a heart transplant unit. *Legionella* had been refractory to conventional sanitation treatments. The incidence of *Legionella* infection confirmed by urine antigen testing approximated 23% before point-of use water filters were installed. After filter installation, as part of the infection control strategy, the rate dropped to 15% and it was further reduced to 1.9% with urine *Legionella* antigen screening and the corresponding use of antibiotics.

Application of sterile filters on faucets and showerheads became part of an infection control program in response to an outbreak of 6 cases of *P. aeruginosa* (2 pneumonias, 2 septicemias and 2 wound infections) in an adult hematology/oncology unit at the University of Bonn in Germany.[173] A survey of 209 environmental samples revealed contamination in surface cleaning equipment, taps, wash basin drains and showers. After implementation of the strategy involving point-of use water filters, the rate of hospital acquired infection reverted to pre-outbreak levels.

Vonberg and co-workers of the Medical School Hannover (Germany) evaluated the performance of 0.2 μm point-of-use tap water filters in 3 intensive care units involving 785 samples.[174] Without filtration, it was shown that over 90% of 32 samples collected were positive for *Legionella* at concentrations ranging from 1–106 CFU/mL. In contrast, 251 samples recovered from taps fitted with filters for 7 days failed to recover any *Legionella* in 250 samples and in the one, the residual concentration was 1 CFU/mL. Despite claims to the contrary, not all filters are alike[175] and confidence in their use should be based upon performance claims and actual clinical use experience.

CONCLUSION

The inadequacy of water treatment standards is being recognized.[176] A greater appreciation is developing for the dangers of water-borne microorganism that survive within, and are released from, the protection of biofilm.[177-179] Drug therapies are being developed to target biofilm.[180-182] Increasing recognition of the role that *Acanthamoeba*, a common water-borne protozoan, plays in protecting bacteria from sanitation methods and increasing the likelihood of passing on the more virulent strains of pathogens contributes to the mounting concern.

Most importantly, the value of microbial protection barriers afforded by 0.2 μm filtration at the point-of-use is gaining momentum with studies such as that by Trautmann and co-workers, in this issue of *FILTRATION,* illustrating the benefit of its use. More aggressive filtration strategies are available to serve as a barrier to viral particles and, with increasing characterization of the magnitude of their effect, such technologies are available and can be implemented easily.

Table 5. Comparison of water treatment methods for the reduction of microbial contamination

Method	Ease of installation	Cost	Maintenance	Efficacy		Disadvantage	Reference numbers
				Short-term	Long-term		
Heat	Easy	Low	Easy	Good	Poor	Failure to maintain consistent temperature Recolonization at low temperature Hard to reach all taps with dead-leg piping and antiscald valves Scalding potential Labor intensive Recontamination occurs in 30-60 days Increase in biofilm sloughing possible May not penetrate biofilm	76, 171, 191, 193
Chlorine	Difficult must hold 10-50 ppm for 12-24 hr, shock method or 1-2 ppm continuous	High	Fair-difficult	Good	Fair	Amoeba, harbingers of bacteria, are resistant to chlorine Recolonization after system disinfection *Legionella* species more resistant to chlorination System corrosion causes pipe leaks and can promote biofilm formation Carcinogenic byproducts (trihalomethanes) Chlorine levels checked frequently Potential resistance of Mycobacteria Does not penetrate into center of established biofilms	25, 76, 166, 171, 194-196
Chlorine dioxide	Fair	Low-Moderate	Fair-Difficult	Good	Poor	Unknown corrosive properties Unknown maintenance of effective concentration in hot water systems Does not penetrate completely into biofilm Costly	193, 197, 198
Monochloramines	Fair	Moderate	Fair-difficult	Good	N/A	More difficult to remove from water than chlorine or chlorine dioxide May not penetrate into biofilm Potential resistance of Mycobacteria Must be removed from water used for dialysis	199-201
Copper-silver ionization	Fair	Low-Moderate	Moderate			Metallic ions added to drinking water Works well only on water with low dissolved solids content Can corrode steel or galvanized pipe Not equally effective for all pathogens	202
UV	Fair, local effect	Moderate	Moderate cleaning for effective energy transmission	Good	Fair	Scale problems Electricians required Poor penetrating power of UV light in established biofilms	148, 149, 151

Table 5. (continued)

Method	Ease of installation	Cost	Maintenance	Efficacy: Short-term	Efficacy: Long-term	Disadvantage	Reference numbers
Ozone	Difficult	High	Moderate	Good	Poor	May cause injured cells Partially degraded organics may enhance biofilm formation Disinfects only at the point of injection Decomposes quickly in hot water Hard to hold effective concentration Specialized equipment required to generate ozone	193
POU filtration	Easy, immediate barrier	Low	Simple	Good	Good	Correct installation essential for bacterial removal	203

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