

Prevention and control of health care-associated waterborne infections in health care facilities

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The current article is a review of the public health risks attributable to waterborne pathogens in health care. The consequences of health care-associated infections (HAIs) are discussed. Not only are *Legionella* spp involved in HAIs, but also *Pseudomonas aeruginosa*, other gram-negative microorganisms, fungi, and amoeba-associated bacteria. This is particularly noteworthy among immunocompromised patients. New prevention strategies and control measures brought about through advanced planning, facility remodelling and reconstruction, disinfection, and filtration have resulted in a significant reduction of the incidence of waterborne HAIs. The positive consequences of a comprehensive multibarrier approach including prevention and control programs in health care facilities are discussed. Environmental cultures are now integrated within the infection control program of some European countries. In high-risk areas, the application of disposable sterile point-of-use filters for faucets and shower heads appears to be the practice of choice to efficiently control waterborne pathogens and to prevent infections. (Am J Infect Control 2005;33:S26-40.)

In developed countries, as many as 5% to 10% of all hospitalized patients contract health care-associated infections (HAIs) each year. These infections prolong hospital lengths of stay and cause significant morbidity, mortality, and financial burden. It has been estimated that 35 million patients are admitted each year to the nearly 7000 acute-care institutions in the United States, and the number of HAIs, with an estimated incidence rate of 5% to 10%, approximates 1.75 to 3.5 million.¹ The dramatic increase in antibiotic resistance is a further risk to be taken into account that may increase these statistics.

To reduce the number of HAIs, we must direct our attention to hospital hygiene, with a 2-fold aim: to undertake a systematic risk assessment by describing, characterizing, and estimating the public health consequences of HAIs and to define the infection

sources and transmission pathways of the causative health care-associated pathogens and to develop risk management strategies to prevent and control HAIs while considering economic, legal, and political issues.

In 1883 in Berlin, Germany, Robert Koch was the first to show high heterotrophic colony counts of bacteria present in tap water.² However, although it has long been established that water plumbing systems and faucets are reservoirs for pathogens, especially gram-negative bacteria such as *Legionella* and *Pseudomonas aeruginosa*, an international consensus concerning prevention and control strategies has still not been developed.³

Anaissie et al³ pointed out that hospital water distribution systems might be the most overlooked, important, and controllable source of HAIs. They estimated that up to 1400 deaths occur annually in the United States as a result of health care-associated pneumonia caused by waterborne *P aeruginosa* alone. Hunter⁴ has criticized this point of view and stated that the disease-related burden due to waterborne transmission of health care-associated pathogens might be overestimated. However, the results of new molecular typing methods are consistent with Anaissie's risk assessment results.⁵ Furthermore, intervention studies have demonstrated a dramatic decrease in the incidence of waterborne infections.⁶

In 2004, the World Health Organization (WHO) issued new guidelines for drinking water quality.⁷ The new guidelines recommend the development of a safety program for water intended for human

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consumption in health care facilities. Similarly, several European countries (the United Kingdom, France, Germany) and the US Centers for Disease Control and Prevention have developed new guidelines for water quality in health care facilities.^{8,9}

This article provides an overview of waterborne health care-associated infections and discusses these prevention guidelines and strategies.

RISK ASSESSMENT

Waterborne pathogens in water distribution systems and consequences for health care facilities

In the WHO Guidelines for Drinking Water Quality, health care facilities are described as hospitals, health centers, hospices, residential care facilities, dental offices, and dialysis centers. In these institutions, water should be suitable for human consumption and for all usual domestic purposes, including personal hygiene.⁷

The WHO stresses that the approach to risk assessment must be systematic, the ecology of waterborne pathogens well known, and all sources and pathways evaluated. WHO insists on the necessity of a comprehensive, multibarrier program to ensure the quality of water for human use.

Waterborne pathogens can be introduced into a health care facility water distribution system from a catch basin or raw water reservoirs or by leakage into the distribution system. Despite water treatment and a chlorine disinfection process (as is currently performed in most countries), water may still contain low concentrations of various microorganisms such as *Legionella*, *P aeruginosa*, pathogenic *Mycobacteria*, *Acinetobacter* spp, *Aeromonas* spp, and *Aspergillus*.⁷ After these microorganisms (gram-negative bacteria in particular) have entered the plumbing system of health care facilities, they can induce the development of biofilms, embedding themselves in a matrix of extracellular organic polymers combined with nonorganic particles. Such biofilms form in most water systems. In the health care facility environment, biofilms may be found in potable water supply piping, hot water tanks, and air conditioning cooling towers as well as in sinks, sink traps, faucet aerators, and shower heads. Biofilms, particularly in water systems, do not present as a continuous slime or a film, but are more often patchy and heterogeneous in nature. They may form under both stagnant and flowing water conditions. Water storage tanks constitute a particular site of concern for biofilm development, especially if the water temperature is in the proper range to permit the growth of thermophilic bacteria. Biofilm formation in water systems is affected by different parameters such as

water chemistry, flow, stagnation, materials of pipe construction, degree of pipe corrosion, high water shear stress, and flushing.^{8,10,11}

Although algae, protozoa, and fungi may be present in biofilms, the predominant microorganisms responsible for biofilm formation in water systems are gram-negative bacteria. Certain biofilm-forming bacteria (eg, *Legionella*, *Klebsiella*, *Pantoea agglomerans*, and *Enterobacter cloacae*) can also be etiologic agents of HAIs. In addition, biofilm-forming organisms are more resistant to both antibiotics and disinfectants than are planktonic (free-floating) organisms, either because their cells are protected by the extracellular polymer matrix or because they are physiologically different.⁸

When conditions are optimal for biofilm-producing microorganisms, a thick biofilm can be produced in less than 7 days (Fig 1).

In a typical water distribution system, water runs continually through the larger-diameter supply pipes. This limits microbial bioburden accumulation.¹⁰ However, as water is distributed into downstream pipes of smaller and smaller diameter, biofilms can develop to a considerably greater extent because of the greater degree of water flow variability to which these pipes are exposed as a consequence of varying patterns of water use. When formed at or near the point of use, a biofilm community can act as microbial repository that constantly disperses viable microbes into the passing water stream. These microbes can then colonize patients, caregivers, environmental surfaces, medical devices, and instruments that subsequently come into contact with water.¹⁰ In addition, tap water used for cleaning can contaminate a wide range of surfaces that in turn become reservoirs of infection, such as work surfaces, utensils, and sponges. Tap water may also contact and contaminate indwelling medical devices, mouth wash solutions, dental water lines, solutions for therapeutic use, antiseptics, surface and instrument disinfectants, endoscopes, dialysis machines, nebulizers, humidifiers, ventilators, faucet aerators, showers, eyewash stations, and even cooling towers and evaporative condensers. Recent reports have shown that nontouch or sensor-operated hospital faucets can also be a possible source of *P aeruginosa* and *Legionella* spp.^{6,13}

Fig 2 depicts a comprehensive view of water pathways in health care facilities, from catch basin to points of use.¹⁴

According to the WHO guidelines, hospitals, nursing homes, other health care facilities, schools, hotels, and other large buildings are all high-risk environments, both because of the complex nature of their drinking water systems and because of the sensitivity of their occupants.⁷

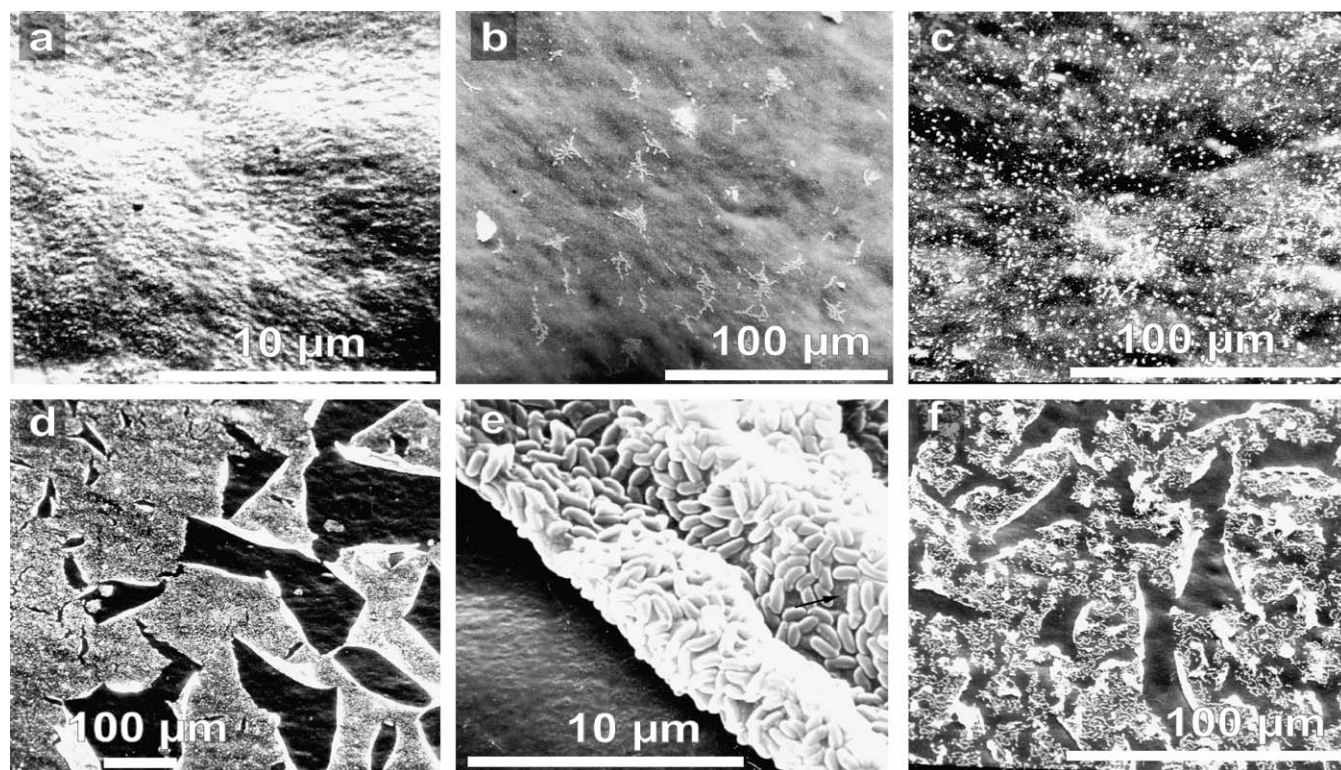


Fig 1. Induction of a biofilm by running drinking water through a silicone tube (inner tube diameter 4 mm). **a**, Inner surface of the control tube without biofilm. **b**, Microcolonies appear after running drinking water for 2 days. **c**, Numerous microcolonies appear after running drinking water for 4 days. **d**, Surface covered with biofilm (disrupted by preparation) after running drinking water for 7 days. **e**, Magnification of **d**. Numerous microorganisms embedded in an extracellular matrix (arrow). **f**, Surface covered with biofilm after running drinking water for 15 days.¹²

Waterborne pathogens in health care facilities

In conformity with the Water Safety Plan proposed in the WHO Guidelines for Drinking Water Quality, a systematic risk assessment should be conducted with a multistep approach that should place special emphasis on the identification of relevant pathogens, knowledge of their infecting pathways (from source to consumer/patient), and their public health consequences. The following steps must be included:

1. Hazard identification
2. Exposure assessment
3. Dose-response assessment
4. Risk characterization combined with knowledge of ecologic criteria (eg, identification of the source and reservoirs of waterborne pathogens in the distribution system)

As mentioned in the WHO Guidelines for Drinking Water Quality, besides disease transmission by ingestion of drinking water, waterborne disease can also be transmitted by inhalation of droplets or by contact with tap water. All these transmission pathways are important and must be controlled.

Furthermore, the guidelines state that the safety of drinking water does not only relate to pathogens transmitted by the fecal-oral route but also to other pathogens such as *Legionella* spp and *P aeruginosa*. Fig 3 depicts the transmission pathways of the most relevant waterborne pathogens.⁷ This new approach, which focuses not only on fecal-oral transmission of waterborne pathogens but also on transmission pathways of other pathogens, is important and has great consequences for water safety strategies in health care facilities, especially concerning the prevention and control of the opportunistic and waterborne pathogens so often found in health care facilities.

The risk of infection by opportunistic pathogens (eg, enterohemorrhagic *Escherichia coli*, Norovirus, *Campylobacter*) results from a dynamic interaction between microbe and host. For an infection to occur, the target organ must come in contact with a sufficient amount of microorganisms, these microorganisms must possess specific virulence factors, these virulence factors must be expressed, and the defenses of the organ system first hit must be overcome.

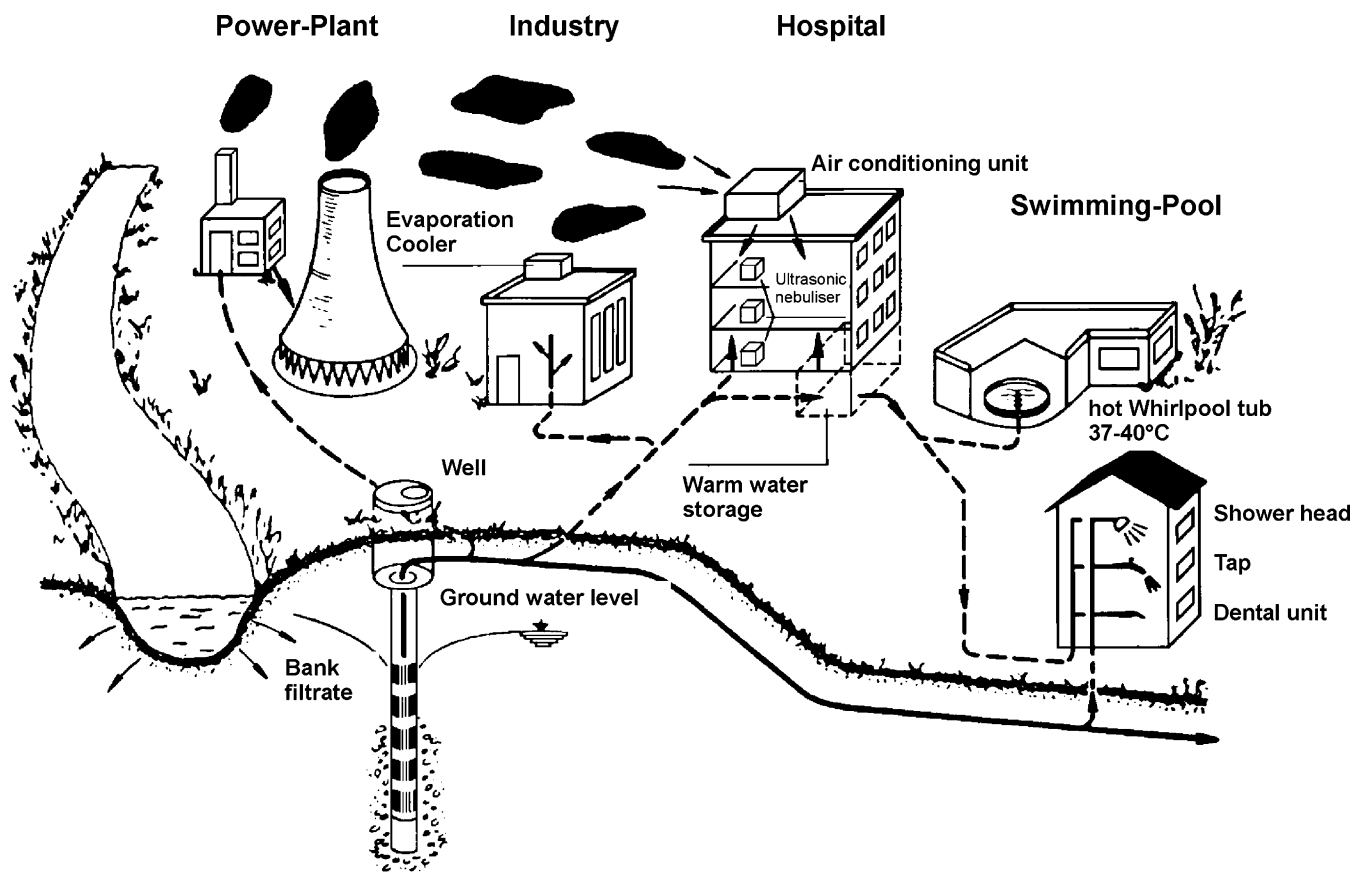


Fig 2. Comprehensive view of a water distribution system from catch basin to water outlets, cooling towers, and other reservoirs for waterborne pathogens (Exner M, Schulze-Röbbecke R. Legionellen-Epidemiologie, Ökologie, Infektionsquellen und präventive Massnahmen Öff. Ges Wes 1987;49:90-6.)

Theoretically, the risk can be estimated as follows:

Risk of infection

$$= \frac{\text{No. of microbes} \times \text{Virulence factors of microbes}^{15,16}}{\text{Specific immunologic status of host target organ}}$$

The formula does not express a quantitative result; it rather gives us a theoretic idea about the strength of all determinants of infection, where the denominator (eg, immunosuppressed vs healthy individual) is opposed to the numerators (eg, a very virulent microbe requires a comparatively smaller number of organisms to infect).

The development of a control strategy of waterborne pathogens must be based on two aspects:

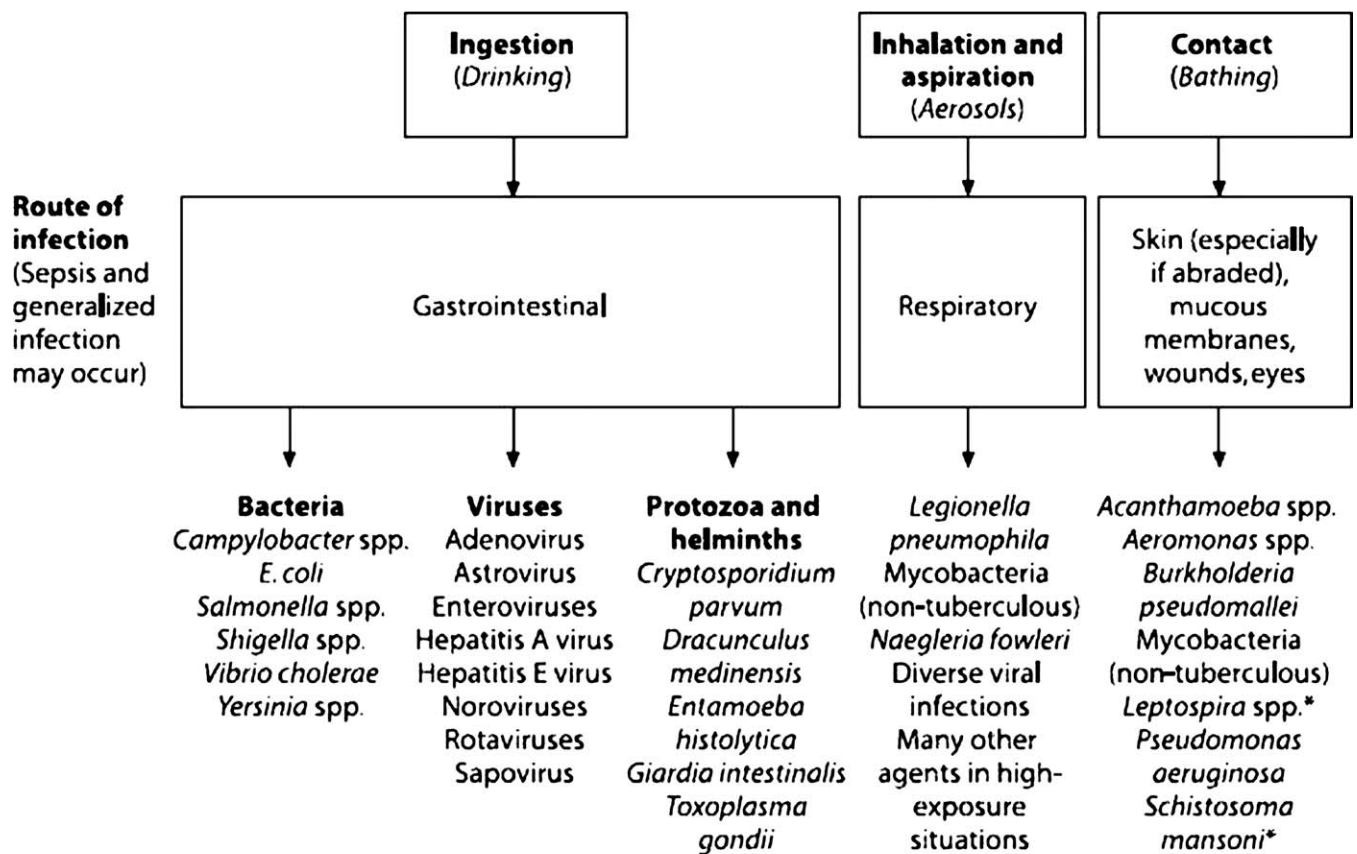
1. the reduction of the number of microbes that can harm the patient and
2. the specific protection of patients at high risk for infection.

The waterborne pathogens of particular significance in health care facilities are the following:

- *Legionella pneumophila* and other *Legionella* spp
- *P aeruginosa*
- Other gram-negative bacteria (ubiquitous and water associated)
- Other amoeba-associated bacteria
- Mycobacteria
- Fungi

It should also be mentioned that the list of known water-transmissible pathogens is continuously expanding as new or previously unrecognized pathogens continue to be discovered.⁷

***L pneumophila* and other *Legionella* spp.** *L pneumophila* has been recognized as the first emerging waterborne pathogen not primarily transmitted by ingestion or direct contact but rather by inhalation or aspiration. Furthermore, its presence in water is not revealed by the classic indicators such as colony-forming units (cfu), *E coli*, or coliforms.^{7,14,17} The natural mode of transmission (inhalation or aspiration) particularly places at risk patients with chronic lung disease and those who undergo general anaesthesia. The greatest incidence of *Legionella* infection is found in patients with



* Primarily from contact with highly contaminated surface waters.

Fig 3. Water-related pathogens and their disease transmission pathways.

heart transplants, with corticosteroid administration an additional risk factor. For patients with predisposing risk factors, there is not only a higher risk of infection (up to 50%, as a consequence of their own immunosuppressive or predisposing status) but also a higher incidence of lethality than in other settings.¹⁸ Consequently, hospitals and residential institutions must pay particular attention to the prevention of legionellosis.

Health care-associated *Legionella* diseases are classified into two groups:

1. Diagnosed health care-associated legionellosis in a person who was in the hospital 10 days before the onset of symptoms.
2. Probable health care-associated legionellosis in a person who was in a hospital for a period of between 1 and 9 days, 10 days before the onset of symptoms, and who either became ill in a hospital involved with one or more previous cases of legionellosis or from whom an isolate was obtained that was found to be identical to isolates obtained at the same time from the hospital water system.¹⁹

Compared with other forms of contracting a *Legionella* infection, community-acquired legionellosis represents the highest percentage of all notified *Legionella* diseases in Western countries. In Germany, a new multicenter study showed that up to 5% of all cases of community-acquired pneumonia were caused by *Legionella*. It is estimated that 5% to 20% of notified legionellosis are of health care-associated origin.¹⁹ Mortality rates range from less than 1% to as high as 18%, depending on factors such as the underlying health status of the patient, the promptness of a specific therapy, and whether the disease is sporadic, health care associated, or part of a large outbreak. An untreated HAI in patients with severe underlying diseases can seriously increase mortality. In the last few years, the percentage of health care-associated cases decreased regularly and significantly in France (from 20% of all notified legionellosis in 2000 to 9% in 2003), while during the same period the percentage of cases reported for hotels and recreational camp grounds increased from 9% to 13%.¹⁹ These statistics reflect the positive impact of measures taken by health institutions to control the risk of Legionnaires' disease

following the distribution of a ministerial circular in 1998, in which preventive measures (including environmental sampling and cultures) were proposed. The largest outbreak of legionellosis ever reported occurred from June to July 2001 in Murcia, Spain, in which 449 cases were confirmed. An epidemiologic and microbiologic investigation identified the air conditioning cooling towers of the city hospital as the source of the epidemic.²⁰

In summary, health care-associated cases constitute only a small proportion of all reported cases of legionellosis. On the other hand, the rate of health care-associated case mortality tends to be much higher than that of community-acquired cases. As relates to reservoirs and transmission, the reservoirs of community-acquired Legionnaires' disease have been well described. In hospitals, ambulatory care settings, and nursing home settings, there are specific reservoirs such as respiratory devices, humidifiers filled with tap water, and water for bathing, for which HAI evidence has been accumulated and epidemiologic-based associations have been established. In high-risk areas such as hospitals and nursing homes, other reservoirs with unclear epidemiologic links have been cited (eg, mineral water dispensers and water cooling systems in dental units).¹⁹

The risk of health care-associated legionellosis attributed to the colonization of hot and cold water by *Legionella* is well established. Joly et al²¹ performed a 9-month follow-up study at 10 hospitals colonized with *Legionella* and 10 hospitals that were *Legionella* free. They found Legionnaires' disease significantly more often in colonized hospitals than in noncolonized hospitals ($P = .054$). A further 5-year prospective study was conducted at 20 hospitals in Spain to analyze the incidence of new cases of health care-associated legionellosis. Health care-associated legionellosis was diagnosed in 64.7% of the hospitals with *Legionella*-positive water cultures, whereas in hospitals with negative water cultures no health care-associated legionellosis was reported. Because environmental studies have increased the index of suspicion for health care-associated legionellosis, its actual incidence has automatically and significantly increased.²² Kool et al²³ performed a retrospective review of microbiologic and serologic data from the laboratories of the hospitals. After extensive modification of the water system, no further cases of *Legionella* could be identified. The authors concluded that *Legionella* can colonize hospital plumbing water systems for long periods of time, resulting in a continuing risk for patients, especially for those who are immunocompromised. The percentage of distal sites in the water system of a hospital that are positive for *Legionella* directly correlates with the incidence of Legionnaires'

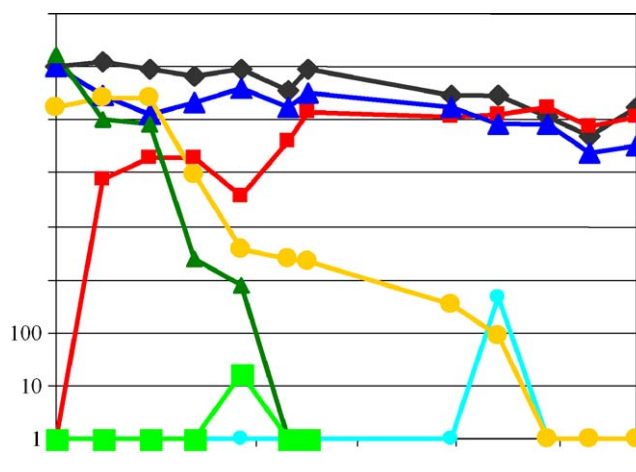


Fig 4. Survival of bacteria in established biofilms exposed to different disinfection treatments and the effects of chlorine, chlorine dioxide, and ultraviolet C on the formation of new biofilms in silicone tubes. Dark diamonds, Old biofilm, untreated; dark squares, new silicone tube, untreated; dark triangles, old biofilm plus ultraviolet; light diamonds, new silicone tube plus ultraviolet; light squares, old biofilm plus chlorine; light triangles, old biofilm plus chlorine dioxide; large squares, new silicone tube plus chlorine dioxide.

disease, namely, that the greater the percentage of sites holding *Legionella*, the more likely that fatal cases will occur. The opposite is also true, namely that if there is no *Legionella* in the water supply, the probability that fatal cases will occur is minimal.^{24,25}

On the basis of evidence that a link exists between the colonization of hot and cold water systems in hospitals and other buildings, the risk of a *Legionella* infection must be assumed to exist not only at points of use within a particular building but also in the entire water delivery system. Exner et al^{26,27} investigated hospitals and residential units and other buildings that could be affected by the colonization of the water system with *Legionella*. They distinguished between local and systemic colonization of the water system.

Local or nonsystemic colonization was defined as colonization of isolated parts of the plumbing system (eg, water faucets or shower heads). *Systemic* colonization was defined as colonization of the whole system, including the central parts of the water supply.

In the case of local or nonsystemic colonization, it is possible to flush out *Legionella* from distal water sites (eg, water faucets). However, in cases of water distribution system colonization, even intensive system flushing would have no effect on the reduction of *Legionella*. In 1993, an investigation of legionellosis in German buildings revealed that up to 43% of hospitals had a systemic colonization.²⁷

The presence of *Legionella* in the plumbing system of a hospital can originate from the municipal water distribution network. Lawrence et al²⁸ characterized a set of 75 clinical *L pneumophila* isolates with no apparent epidemiologic link obtained from 24 hospitals in Paris, France, during the period 1991-1997. Unexpectedly, 25 clinical isolates from 15 hospitals had an identical profile, as revealed by polymerase chain reaction and pulse-field gel electrophoresis. The same profile was subsequently found in 16 of 64 randomly selected environmental *L pneumophila* serogroup 1 isolates from 15 different sites in the Paris area. There was no evidence of a geographic clustering or of an incidence peak of these isolates. Similar results have also been obtained by Köhler et al.²⁹ Interesting fact: the type A first found in the water distribution network of Paris has meanwhile spread to other cities, namely, in South France, suggesting that a particular type of *L pneumophila* serogroup 1 might be present in France.

After bacteria have entered the plumbing system, risk factors for multiplication and persistence like piping materials of construction, areas of stagnation, and temperature (>20°C to 50°C) play a determining role. Consequently, one has to assume that a continuous risk of penetration of new *Legionella* species into the plumbing system of a hospital exists. Control measures should begin with technical requirements for the planning and avoidance of water flow stagnation, temperature control, and disinfection. Disinfection methods include heat, ultraviolet light, chlorination/hyperchlorination, and copper-silver ionization.³⁰⁻³⁷ Each of these disinfection methods have their unique requirements. For instance, ultraviolet light can only be efficient if the plumbing system was not contaminated with *Legionella* before it was installed.³⁴

The ability of point-of-use filters to eliminate *Legionella* and other pathogens from water was shown by Sheffer et al.³⁸ The authors concluded that disposable point-of-use filters completely eliminated *L pneumophila* and *M gordonae* from hot water samples. They can also be used to prevent the exposure of high-risk patients to waterborne pathogens without modification or disinfection of the potable water system. Therefore, French, German, Italian, and UK hospitals now apply these point-of-use filters in several of their high-risk areas. Point-of-use filters provide a high degree of security, as will be discussed later in this review.

Factors that enhance colonization and multiplication of *Legionella* in man-made environments include (1) temperature range of 25-42°C, (2) water stagnation, (3) scale and sediment, and (4) presence of certain free-living aquatic amoebae that can support the intracellular growth of *Legionella*.¹⁰

In the United States, monochloramines are sometimes used for the treatment of public drinking water,

which may reduce the risk of health care-associated Legionnaires' disease. However, methods of municipal water disinfection vary from country to country.²⁵ In Germany, for example, monochloramines are forbidden because of toxicologic considerations.

A further important step in validating and verifying the quality of the plumbing system is to obtain routine environmental cultures of *Legionella* from the water system. There is an international discussion about the utility of this approach.^{18,22,24,26,38,39} The US Centers for Disease Control and Prevention (CDC) does not make recommendations regarding routine culturing of water systems in health care facilities that do not have patient care areas for persons at high risk for a *Legionella* infection.⁸ However, experts in the field of waterborne microbes, governmental agencies, and professional organizations advocate routine culturing of *Legionella*, arguing that knowledge of the environmental presence of the bacterium can direct monitoring for disease and that remediation may prevent disease. Moreover, environmental monitoring followed by clinical surveillance has been successful, permitting the discovery of previously unrecognized cases of health care-associated Legionnaires' disease. The approach proposed by Stout and Yu³¹ is to periodically culture samples taken from the hospital's tap water system to monitor *Legionella* spp. If >30 % of the samples are found to be positive for *Legionella*, decontamination of potable water is warranted. The premise for this approach is that no cases of health care-associated legionellosis can occur if *Legionella* spp. are not present in the potable water system, whereas cases of health care-associated legionellosis can occur if *Legionella* isolates have been detected in water by routine culture.^{22,24}

In Europe, and particularly in Germany, there is another policy concerning routine culturing, which is based on the Council Directive 98/83/EC on the Quality of Water Intended for Human Consumption. This directive stipulates that no waterborne pathogen should be found in the distribution system in concentrations that can harm the consumer. In France and Germany, environmental culturing for *Legionella* is required by law.^{19,38} In 1990, Exner et al²⁶ were the first to propose recommended concentration values for *Legionella* as a systemic plumbing system contaminant. In their approach, it is not necessary to stay under the 30% contamination level fixed in US recommendations, but rather to control systemic contamination in the plumbing system. The target is to reduce the concentration of *L pneumophila* in the whole water system below the threshold of 1000 cfu/l. In the German approach, the number of water samples taken can be reduced from 10 to 4 samples per building.

In France,¹⁹ the following limit values for *Legionella* concentration in water used in clinical units have been proposed:

- Classical patients, including those with classical individual risk factors (eg, elderly, alcoholism, tobacco use)
 - Target level: <1000 cfu/L *L. pneumophila*
 - Alert level: 1000 cfu/L *L. pneumophila*
 - Maximum level: 10,000 cfu/L *L. pneumophila*
- High-risk patients (eg, severe immunosuppression, transplantation, or under corticosteroid therapy with an equivalent dose of 0.5 mg/kg/d prednisone during 30 days or more or a dose of 5 mg/kg/d during 5 days or more)
 - Target level: <50 cfu/L *Legionella* spp
 - Alert level: 50 cfu/L *Legionella* spp, which corresponds to a single colony per Petri dish, representing 5 L filtered water
- Maximum level: 250 cfu/L *Legionella* spp

The levels have been established in function of the detection limits and the feasibility of the method: 50 is the detection limit and 250 is the analytic/quantification limit (AFNOR, NF T 90-431 is the old norm from 2003, which has just been reviewed now).

The *target level* is defined as the best way to minimize the risk, whereas the *alert level* implies that appropriate health care facility staff members should be informed and that a follow-up study of the procedure for maintenance and new controls is indicated. When the *maximum level* is reached, disinfection procedures must be performed immediately. This approach has not only direct consequences for infection prevention but is also a method for verification and validation of the quality of plumbing system maintenance. In reality, for high-risk patients, a maximum value is not tolerable. The alert level must also be much lower (should theoretically be “complete absence of colony,” but unrealistic to achieve in practice).

In the future, we hope that the environmental culturing of *Legionella* will be incorporated into the water safety program recommended by the WHO as an essential measure of quality assurance.

***P. aeruginosa*.** *P. aeruginosa* is known to be highly endemic in intensive care units (ICUs) and other parts of health care facilities where patients are treated.^{6,42} In ICUs, the organism causes urinary tract infections, surgical wound infections, bacteremia, and pneumonia. In other parts of health care facilities and in the community, *P. aeruginosa* causes dermatitis, otitis externa, and keratitis, and it is known as a swimming pool-associated pathogen. Colonization by *P. aeruginosa* frequently precedes infection. The origin of the organism and the precise mode of transmission have

long been unclear. *P. aeruginosa* is commonly found in moist environments such as plants, soil, and water, particularly in tap water. The association and role of tap water in *Pseudomonas* infections was not clear for a long time. Previous studies failed to recover microorganisms as a result of a suboptimal sampling strategy that did not pay proper attention to sampling the water delivery infrastructure itself, taking multiple samples at different sites and at different times of the day and using the available spectrum of modern genetic typing systems.⁵ Therefore, before the advent of DNA-based typing techniques, it was not suspected that *P. aeruginosa* strains residing in water habitats were the same as those that caused health care-associated infections in patients. However, with the use of new molecular typing techniques, several investigators have shown that a significant proportion of infections in ICUs are caused by strains previously found in water outlets.^{11,13,40-45} Trautmann et al⁶ demonstrated that 39% of strains causing invasive infections in patients originated from water outlets present in the same room. Other recent studies have reached identical conclusions.^{11,13} Blanc et al¹¹ showed that in 42% of cases reported in an ICU, isolates identical to those in the faucets were found. They realized that the water system of the ICU was the primary reservoir for patient colonization and infection with *P. aeruginosa*. This survey demonstrated that the water distribution system may be an important reservoir of health care-associated *P. aeruginosa*, even when the contamination level is low and despite the fact that all testing criteria for drinking water are met. Vallés et al¹³ showed that the source of *P. aeruginosa* causing ICU-acquired colonization was predominantly environmental. Their findings indicated that the tap water in the ICU was the source of the colonization, with more than 60% of the tap water samples contaminated with *P. aeruginosa*. This study is unique in that more than 1600 isolates were examined over a substantial period of time. More than half of evaluated patients were colonized with *P. aeruginosa*, and this colonization was not limited to the respiratory tract. This conclusion was drawn after observing that in most cases the detection of *P. aeruginosa* in water occurred before the detection of a strain from a patient and that the tap water was colonized mainly by the same strain of *P. aeruginosa*. Their results suggest that efforts to prevent colonization by *P. aeruginosa* should be directed toward decontamination of tap water and infection control measures that are targeted to reduce exogenous sources of water contamination.

Contamination of tap water faucets may derive not only from the water distribution system⁴⁶ but also from patients. In our own studies, we determined that as many as 16% of newly installed pipes in the water

distribution system are contaminated with *P aeruginosa*. It is important to note that the presence of *P aeruginosa* is not predicted by classical indicators of water contamination (eg, cfu, *E coli*, coliforms).^{7,11}

One new source of *P aeruginosa* and *Legionella* spp contamination appears to involve the use of “nontouch” water fittings in hospitals. The local contamination of “nontouch” fittings results from the low volume of water that flows through the fitting outlet, the accompanying low water pressure, and the column of water left standing behind the outlet when it is not in use. Because the temperature of that standing water is usually about 35°C, the temperature conditions prove to be quite ideal for the growth of these bacteria.⁴⁷⁻⁴⁹

Anaissie et al⁵ estimated that as many as 1400 deaths occur each year in the United States as a result of waterborne health care-associated pneumonia caused by *P aeruginosa* alone. A new study published by Trautmann et al⁶ has shown that it is possible to reduce HAIs in a surgical intensive care unit by installing disposable point-of-use water filters on all patient-related water outlets.

Other gram-negative bacteria associated with water and moist environments. Other Gram-negative bacteria that are associated with water and HAIs are as follows:

- *Burkholderia cepacia*
- *Stenotrophomonas maltophilia*
- *Sphingomonas* spp
- *Ralstonia pickettii*
- *Serratia marcescens*
- *Acinetobacter* spp
- *Enterobacter* spp^{8,50-52}

These bacteria pose the highest risk of infection to immunocompromised patients. Medical conditions associated with these bacterial agents range from colonization of the respiratory and urinary tracts to deep disseminated infections that can result in pneumonia and blood stream bacteremia.⁸ Colonization by any of these organisms often precedes the onset of infection. The use of tap water in medical care (eg, for direct patient care, to dilute solutions, as a water source for medical instruments/equipment, and during the final rinsing stages of instrument disinfection) therefore presents a potential risk of contamination. *Acinetobacter* spp and *Enterobacter* spp are gram-negative bacterial pathogens that can proliferate in moist environments. Members of these genera are responsible for HAIs such as bloodstream infections, pneumonia, and urinary tract infections among medically compromised patients, especially those in ICUs and burn therapy units. *Acinetobacter* spp constitutes a significant clinical problem. The US CDC has reported that the average infection rates are higher from July

through October than from November through June.⁸ Mortality rates from infection rates are higher from July through October than from November through June. Mortality rates from *Acinetobacter* bacteremia range from 17% to 52%, with rates as high as 71% reported for pneumonia caused by infection with either *Acinetobacter* spp or *Pseudomonas* spp.⁸ Multidrug resistance exhibited by *Enterobacter* spp, especially against third-generation cephalosporins, contributes to increased morbidity and mortality.⁸

A dramatic outbreak of *Burkholderia cepacia* bacteremia that was linked to contaminated hospital water used for dilution of an alcohol-based skin antiseptic was described by Nasser et al.⁵² In what appears to have been the largest single source of health care-associated bloodstream infections ever reported, they identified the source of *B cepacia* bloodstream infections during a period of 7 years (411 episodes in 361 patients). It was also the first report of an alcohol-based skin antiseptic contaminated by tap water as source for health care-associated bacteraemia. *B cepacia* bloodstream infections afflicted 2.6 to 7.1 patients per 1000 discharges during the years studied, often accompanied by substantial morbidity.

Some of the previously mentioned pathogens can be found in surface water and can survive and multiply in municipal water distribution systems. In 2003, there was a sharp increase of *E cloacae* in the surface water of some drinking water reservoirs in Germany during the months of September and October, which could only be detected with use of a commercially available microbial identification system (Exner, unpublished data). At one drinking water utility, *E cloacae* complex was still found in low concentrations after disinfection treatment of the water distribution system. Like *P aeruginosa*, these microorganisms have the potential to form biofilms.⁸

The disinfection methods used to control these microorganisms are the same as those routinely implemented for *Legionella* and *P aeruginosa*. In the event of a disease outbreak involving one of these microorganisms, tap water must be regarded as a potential reservoir of infection and should be promptly investigated in the same way as is recommended for *P aeruginosa* and *Legionella*.

Nontuberculous mycobacteria. Nontuberculous mycobacteria (NTM) are also called pathogenic environmental mycobacteria (PEM). They were previously named “atypical mycobacteria” or “mycobacteria other than *Mycobacterium tuberculosis*.” They are classified in three groups: rapidly growing, intermediately growing, and slowly growing mycobacteria.⁵³

The major clinical syndromes associated with nontuberculous mycobacterial infections are skin and soft

tissue diseases, chronic bronchopulmonary disease, cervical/other lymphadenitis, disseminated infection, and catheter-related infections. Water-associated nontuberculous mycobacterial infections or colonizations involve the following organisms: *M abscessus*, *M avium* complex (MAC), *M chelonae*, *M fortuitum*, *M marinum*, *M ulcerans*, *M simiae*, *M mucogenicum*, and *M xenopii*.⁵³⁻⁵⁶

In addition to HAI outbreaks, NTM can colonize patients in health care facilities through consumption of contaminated water and ice or through inhalation of water aerosols. Patients may yield positive sputum cultures even in the absence of a clinical disease. Using tap water during patient procedures, for specimen collection, or in the final steps of instrument reprocessing can result in NTM "pseudocontamination outbreaks."

Three outbreaks of health care-associated NTM infections were described in 2004. A first outbreak of bacteremia was caused by *M mucogenicum* in a hospital water supply.⁵⁷ A second outbreak involved *M simiae*, also associated with the hospital water supply.⁵⁸ In France, *M xenopii* has been responsible for 50 to 60 bone infections following the contamination of endoscopic surgical material with rinsing water (Clinique du Sport, Paris).

The first bacteremia outbreak of *M mucogenicum* was reported in a bone marrow transplant unit and in an oncology ward, apparently after water contamination of central venous catheters during bathing/washing. Nontuberculous mycobacteria were isolated from several water sources at the institution (water faucets, shower heads, hospital hot water) and also in the municipal water supply to the hospital. This outbreak appears to have been associated with a reduction in chlorine levels within the municipal water distribution system.

In the second outbreak, *M simiae* was identified in water samples from the hospital, showers in the homes of patients, and from a well supplying water to the hospital. The same single clone was predominant among water isolates and patient isolates.⁵⁸

Schulze-Röbbecke et al^{54,55} detected mycobacteria in 80% to 90% of surface water samples and in tap water samples at concentrations up to 1000 cfu/L. After water utility treatment (filtration and disinfection), they noted a two-log reduction in mycobacteria concentration. However, regrowth of mycobacteria in the municipal water distribution system occurred, restoring mycobacterial concentrations to pretreatment levels. There were no physical, chemical, or microbiologic parameters that could be correlated with NTM concentrations. The optimal temperature for NTM growth ranged from -10 to +20°C (14-68°F). NTM showed a high resistance to chlorine and were able to tolerate free chlorine concentrations normally found at the

faucet (0.05-0.2 mg/L). Mycobacteria are 2 to 100 times more resistant to chlorine than coliforms. Their ability to form biofilms at fluid/surface interfaces contributes to their resistance to chemical inactivation and provides them with an adapted microenvironment for their persistence and proliferation. Even copper-silver ionization of the water did not eliminate *M simiae*.⁵⁸ Bathing or showering with a central venous catheter (CVC) seems to be a high risk factor that should be avoided. Although the recommendation was made that high-risk patients (eg, patients with acquired immunodeficiency syndrome) should not take showers, such a recommendation is not consistent with patients maintaining as normal a quality of life as possible. Because the risk of NTM does not seem to be controllable by classical disinfection procedures, point-of-use filters remain the solution of choice. They protect high-risk patients while allowing them to maintain quality of life.⁵⁹

Fungi

Filamentous fungi such as *Aspergillus* spp, *Penicillium* spp, and *Fusarium* spp have a high and life-threatening significance for patients with altered immunity, particularly neutropenic patients and those with reduced pulmonary health defenses (eg, patients taking corticosteroids). Patients with severe neutropenia are at high risk for invasive aspergillosis. Other patients at high risk for invasive aspergillosis include those undergoing organ and bone marrow transplantation and those receiving corticosteroids or other newer immunosuppressive therapies.^{5,8,60-62} In patients undergoing hematopoietic stem cell or bone marrow transplantation, a recent increase in the incidence of invasive aspergillosis has been reported. In their last study, Anaissie et al^{61,62} observed a high level of recovery for fungi extracted from water. *Aspergillus* spp and *Penicillium* spp were the two most common fungi identified from municipal water and from hospital water. The organisms that colonized the hospital water distribution system (*Aspergillus* spp and other pathogenic fungi) were the same species as those isolated from municipal water and other water-related hospital buildings. These fungi become part of the biofilm that forms in the pipes of the hospital water system. A strong correlation exists between the type and isolation frequency of fungi isolated from hospital water and those detected in hospital air.^{61,62} The authors brought to light that hospital water distribution systems may be potential indoor reservoirs of *Aspergillus* spp and other fungi, which could eventually come into contact with patients through aerosolization of fungal spores. Although further investigation will be required to substantiate the finding, this study

indicated that fungi appear to use the same unique mechanism to colonize water distribution systems.

Fungi are also brought into health care facility water plumbing systems through the municipal water distribution system and can be constituents of biofilm microflora.⁶⁰

To protect high-risk patients, it is advisable to install point-of-use filtration systems. Further studies involving waterborne fungi should provide more insight into the role of surface water reservoirs, the correlation (if any) of their presence in water with that of indicator bacteria, and on the efficacy of disinfection.

Other amoeba-associated bacteria

Free-living amoebae are known as a host reservoir for many aquatic bacteria that contaminate water supplies.⁶³⁻⁶⁷ To evaluate the role of amoeba-associated bacteria as etiologic agents of ventilator associated pneumonia (VAP), La Scolla et al⁶⁴⁻⁶⁶ tested the water from an ICU every week for 6 months and attempted to isolate amoeba-associated bacteria. In parallel, serum and bronchoalveolar lavage (BAL) samples were also obtained from 30 ICU patients. A total of 310 amoeba-associated bacteria belonging to ten different species were isolated. The most common bacteria were *Legionella anisa* and *Bosea massiliensis*. DNA from amoeba-associated bacteria was detected in BAL samples from 2 patients, whose samples later seroconverted. Seroconversion was significantly correlated with both VAP and systemic inflammatory response syndrome, especially in patients for whom no etiologic agent had been found by routine microbiologic investigation. Water-related amoeba-associated bacteria might be a cause of VAP in ICUs, especially when routine microbiologic samples are negative. The authors speculated that amoeba-associated bacteria in the environment of intubated patients can cause unexplained infections and outbreaks. The research of new etiologic agents of pneumonia in ICUs should include an environmental study of each ICU and focus on amoeba ecologic findings.

DISINFECTION AND CONTROL OF BIOFILMS

The control of biofilms is crucial for the prevention and control of waterborne pathogens in hospital water supply systems. Because biofilms are difficult to eliminate once established, it is important to prevent their formation by reducing the level of planktonic (free-floating) bacteria in the water supply system and by performing reliable and continuous disinfection of the water supply.

With the help of a silicone tube model that permits the rapid development of biofilms in a running water system,⁶⁸ we investigated the effect and efficacy of different chemicals such as chlorine and chlorine

dioxide on biofilms. Fig 4 shows the survival of bacteria in both untreated biofilms and biofilms exposed to chlorine (constant concentration of 0.3 mg/L), chlorine dioxide (constant concentration of 0.2 mg/L), and ultraviolet C irradiation (long-wave ultraviolet light of wavelengths in the range of 315-400 nm), respectively, and illustrates the formation of biofilms in new silicone tubes under different conditions.

The following conclusions may be drawn from these experiments:

- Under laboratory conditions, permanent exposure to chlorine or chlorine dioxide prevents the formation of a new biofilm. Ultraviolet irradiation of water can also prevent the formation of new biofilm.
- Continual exposure to chlorine (0.3 mg/L for at least 180 days) or chlorine dioxide (0.2 mg/L for at least 70 days) eliminates bacteria embedded in a biofilm without completely eliminating the biofilm itself, even after a prolonged period (60-170 days) of exposure. Ultraviolet irradiation, on the other hand, will not have a significant effect on the level of bacteria in the existing biofilm.
- All the disinfection treatments tested virtually eliminated the dissemination of bacteria from the treated biofilm.
- Morphologically, exposure to chlorine or chlorine dioxide renders a biofilm thinner and denser.

The continuous application of low concentrations of disinfectants and ultraviolet irradiation prevent the formation of biofilms in plumbing systems. Satisfactory results are also obtained with copper-silver ionization,³¹ chlorine dioxide,³² and ultraviolet light disinfection.³⁴ It is important to use disinfectants or ultraviolet light in the water main of new buildings before a biofilm develops. To prevent the formation of biofilms in newly installed water distribution systems, it is also essential to use water treated with chlorine dioxide right from the beginning, as it appears to be the most efficient chemical treatment to remove and prevent biofilms.

However, it should be noted that all systemic water disinfection treatment technologies do not respond effectively to sudden, unanticipated infusions of high concentrations of microbial pathogens because of municipal water system breakdown and repair activities, facility renovation projects, and seasonal water quality variations.

PREVENTION AND CONTROL STRATEGIES

Data collected from outbreak investigations, experimental studies, and studies with molecular typing systems have demonstrated a strong association between pathogens in the water distribution system of health care facilities and HAIs other than legionellosis.

Strategies to prevent and control waterborne pathogens in health care facilities must be based on a comprehensive approach. The development of the most effective strategies will take the following points into account:

- Because the association between waterborne pathogens and HAIs has not been well known until now,⁶⁹ a strong education strategy will be essential to communicate new information to all people involved in water utilities, building architecture, hospitals, etc.
- Clinicians, infection control practitioners, risk managers, facilities engineers, and other professionals involved in health care must be aware of the fact that plumbing systems and water outlets are now regarded as important reservoirs of infection.
- Complete prevention of the penetration of waterborne pathogens into the hospital water supply may be regarded as unattainable. However, the risk can be minimized by filtration and disinfection processes.
- It is known that new pipes in the water distribution system of water utilities can constitute an infection source of *P aeruginosa*. Therefore, such pipes should only be put into service when *P aeruginosa* has not been detected through prior water sampling (0 cfu/100 mL of water).
- Much more information must be obtained before the whole dynamic between surface water reservoirs and pathogens such as fungi and gram-negative microorganisms can be understood.
- In some European countries such as the Netherlands and Germany, most water utilities do not use chlorine to disinfect water in their distribution systems. There is a need to investigate the consequences of different approaches to water treatment with regard to the risk attributable to waterborne pathogens in health care facilities.
- When planning the construction of the water supply system of a new health care facility, it is essential to avoid the development of biofilms. This can be achieved by emptying water lines that are not in service and by preventing water stagnation in the water distribution system.
- The installation of disinfection systems such as copper/silver ionization, chlorine dioxide, chlorine, and ultraviolet light irradiation may prevent the formation of biofilms, but preventing biofilm formation is only attainable if these disinfection systems are placed into operation from the first moment of water flow into the plumbing system.
- If biofilms have developed in a hospital plumbing system, it appears to be very difficult to subsequently bring their formation completely under control.
- In the case of preexisting biofilms, ultraviolet irradiation at the source of water entry into the hospital water system will not have any positive effect on biofilm control.
- In an experimental model, it was possible to eliminate bacteria embedded in a biofilm by the continual addition of chlorine or chlorine dioxide over an extended period of time (60-170 days). However, the probability of attaining complete elimination of biofilms from the plumbing system is extremely low.
- Strategies to prevent biofilm formation must be stringent.
- Chlorine dioxide appears to be more efficient than chlorine alone in removing existing biofilms and preventing the formation of new biofilms.
- Monochloroamines have been proposed as an alternative disinfection method in the United States. However, in some European countries such as Germany, monochloroamines are not allowed for disinfection of water because of toxicologic considerations.
- An important strategic step in the control of waterborne pathogens is control of systemic contamination of the plumbing system. If systemic contamination by *Legionella* and other waterborne pathogens exists, it will not be possible to flush them from water outlets.
- Much greater attention must be paid to the possible contamination of water outlets. Nontouch fittings in hospitals have been identified as possible sources of *P aeruginosa* and *Legionella* spp. This alarming situation must be controlled through the development of technical procedures to reduce and/or eliminate contamination of nontouch fittings.
- The use of sterile water for high-risk patients was proposed by Anaissie et al.³ However, this strategy has limitations, especially when it is necessary for patients to take showers. Sterile bottled water is also much more expensive than water filtration with disposable point-of-use filters.⁶⁹ Risks and consequences for patients must be weighed.
- The application of sterile point-of-use filters on faucets and shower heads has become a part of the infection control program not only for the prevention of *Legionella* but also of *P aeruginosa* infections.
- The results of the efficacy of disposable 0.2- μ m point-of-use filters in experimental investigations and in prospective epidemiologic clinical studies are overwhelmingly positive. In high-risk areas (including ICUs) the installation of disposable point-of-use filters on faucets and shower heads has proved to be effective in preventing and controlling infections associated with waterborne pathogens.^{6,59,69,70}
- The discussion concerning whether to perform environmental cultures should be brought to conclusion in the near future. The purposes of environmental cultures are as follows: (1) to provide

information about the status of the contamination of a plumbing system with different waterborne pathogens and (2) to permit verification and validation of the quality of the control measures applied. The results published by Sabria et al²² support this quite convincingly.

- In the case of systemic contamination from *Legionella* or *P. aeruginosa*, clinicians should be promptly informed that there is an infection risk which should be recognized. In Germany and France, the control of water plumbing systems by environmental cultures is now an integrated part of the infection control program.
- Surveillance for infections from *Legionella*, *P. aeruginosa*, and other waterborne pathogens is important. If there is a high incidence or an increase in infections attributable to these microorganisms, the water system must be considered as an infection reservoir, and control measures must be introduced.
- More information is necessary concerning the consequences of water contamination by fungi and amoeba-associated bacteria. Our current knowledge of these pathogens underscores the contribution of water to their appearance as pathogens in the health care setting.

The knowledge accumulated in recent years supporting the association between waterborne pathogens and HAIs has reinforced the notion that there remains tremendous untapped potential to reduce HAIs previously viewed as inevitable and unavoidable through intervention and preventive measures. The new multi-barrier comprehensive strategy of prevention and control can have huge consequences for patient safety as well as positive economic consequences.⁶⁹

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