

# The Hospital Water Supply as a Source of Nosocomial Infections

## A Plea for Action

Elias J. Anaissie, MD; Scott R. Penzak, PharmD; M. Cecilia Dignani, MD

**Background:** Microbiologically contaminated drinking water is a cause of community-acquired infection, and guidelines for prevention of such infections have been established. Microbes in hospital water can also cause nosocomial infection, yet guidelines for preventing such infections do not exist. The purpose of this review is to assess the magnitude of the problem caused by waterborne nosocomial infections and to plea for immediate action for their prevention.

**Methods:** We conducted a MEDLINE search of the literature published between January 1, 1966, and December 31, 2001.

**Study Selection and Data Extraction:** Investigations in which microorganisms (other than *Legionella* species) caused waterborne nosocomial infections and public health agency recommendations for drinking water.

**Results:** Forty-three outbreaks of waterborne nosocomial infections have been reported, and an estimated 1400

deaths occur each year in the United States as a result of waterborne nosocomial pneumonias caused by *Pseudomonas aeruginosa* alone. Despite the availability of effective control measures, no clear guidelines exist for the prevention of these infections. By contrast, guidelines for the prevention of community-acquired waterborne infections are now routinely used. Hospitals caring for patients at high risk for infection do not enforce the standards of water quality recommended by US and United Kingdom public health agencies for the patients' community counterparts.

**Conclusion:** Because of the seriousness of these nosocomial waterborne infections and the availability, low cost, and proven effectiveness of sterile water, we recommend that hospitalized patients at high risk for infection avoid exposure to hospital water and use sterile water instead.

*Arch Intern Med.* 2002;162:1483-1492

**E**ACH YEAR in the United States, more than 2 million nosocomial infections occur in as many as 10% of all hospitalized patients, causing significant morbidity, mortality, and financial burden.<sup>1-3</sup> In addition, the use of antibiotics to treat these infections leads to increased resistance.<sup>4,5</sup> These infections tend to occur more commonly in immunocompromised patients.<sup>6</sup> Although numerous hospital sources cause nosocomial outbreaks, perhaps the most overlooked, important, and controllable source of nosocomial pathogens is hospital water.<sup>7-9</sup>

The ability of microbes to survive in hospital water tanks was described more than 30 years ago,<sup>10</sup> and numerous studies<sup>11-52</sup> have identified water as a source of nosocomial infection. These organisms can acquire and subsequently transfer antimicrobial resistance<sup>53</sup> and can produce toxins, as demonstrated in a recent catastrophic outbreak secondary to contami-

nation of hemodialysis water (110 cases and 43 deaths).<sup>54</sup> Despite the large number of waterborne nosocomial outbreaks,<sup>11-52</sup> no hospital guidelines exist for their prevention.

This article describes the extent of waterborne nosocomial infections and their mode of transmission and recommends guidelines for their prevention.

## RESULTS

### TYPES OF PATHOGENS AND INFECTIONS

#### *Legionella pneumophila*

Of all the water-related pathogens, *L pneumophila* is most likely to be recognized by health care workers as a cause of nosocomial infection. However, the acquisition of *L pneumophila* infection in the hospital setting is similar to that of other water organisms. The agents of legionellosis and those

From the Myeloma and Transplantation Research Center, University of Arkansas for Medical Sciences, Little Rock.

## MATERIALS AND METHODS

Data sources included peer-reviewed publications located via a MEDLINE database search of keywords *water*, *hospital*, and *infection* in manuscripts published in English between January 1, 1966, and December 31, 2001. All abstracts published between January 1, 1987, and December 31, 2000, at the yearly meetings of the American Society for Microbiology, the Infectious Disease Society of America, and the Society of Healthcare Epidemiology of America were also reviewed. Studies of waterborne nosocomial infections (other than with *Legionella* species) were analyzed for the following: pathogens and their susceptibility patterns, source, site(s) of infection, and method(s) used to link patient and environmental isolates. Reference to legionellosis is made to highlight the similarities that exist between this infection and those caused by other waterborne pathogens. Studies describing infection as a result of colonization of the hospital water supply (as opposed to colonization of distal sites that could have come in contact with water, such as sinks and valves) were the focus of this review. Also reviewed were recommendations for the prevention of waterborne community-acquired infections and recommendations for the prevention of nosocomial pneumonia.

of other nosocomial waterborne infections share remarkable similarities, including (1) their presence and amplification in water reservoirs,<sup>7,8</sup> (2) a strong association with water biofilms,<sup>55</sup> (3) growth requirements (optimal growth at 25°C-45°C, with growth inhibition at higher and lower temperatures),<sup>56</sup> (4) a link between infection with these agents and construction activity,<sup>6,57</sup> and (5) mode of transmission (aerosolization, ingestion, and contact).<sup>9,56,58</sup> Similar to *Legionella* species, these bacteria (including *Pseudomonas aeruginosa*) have also been shown to exist not only in biofilms but also inside free-living amoebae.<sup>59,60</sup> These amoebae harbor the bacteria inside their cysts, giving them a microhabitat and protecting them from disinfectants.<sup>60</sup>

Although recommendations for preventing legionellosis have become standard knowledge in medical textbooks,<sup>58,61</sup> nosocomial waterborne infections by other microbes have been largely ignored despite their high morbidity and mortality rates.<sup>11-52</sup>

### Other Waterborne Pathogens

**Bacteria.** Nosocomial infections caused by waterborne bacteria have been associated with serious morbidity and even mortality and include bacteremias, tracheobronchitis, pneumonias, sinusitis, urinary tract infections, meningitis, wound infections, peritonitis, ocular infections, and others.<sup>11-52</sup> Specifically, *P aeruginosa* can persist in hospital water for extended periods<sup>20</sup> and can cause nosocomial outbreaks,<sup>11-22</sup> frequently with resistant organisms. *Stenotrophomonas maltophilia* is a multidrug-resistant organism that has been implicated in nosocomial waterborne infections.<sup>23-27</sup> Other bacteria associated with waterborne nosocomial infections include species of *Aeromonas*, *Acinetobacter*, *Burkholderia*, *Enterobacter*, *Flavobacterium*, other *Pseudomonas*, *Serra-*

*tia*, and others.<sup>28-41</sup> Overall, these nosocomial waterborne infections were caused by bacteria resistant to at least 2 classes of antimicrobial agents in 13 (76%) of the 17 outbreaks for which susceptibility testing was performed (**Table 1** and **Table 2**).

**Mycobacteria.** Pathogenic mycobacteria have been isolated from hospital water, can persist in water systems over several years,<sup>42</sup> and have been implicated in serious nosocomial outbreaks.<sup>42-50</sup>

**Fungi.** Nosocomial aspergillosis continues to occur despite air filtration, thus suggesting that there may be other hospital sources of spores.<sup>6</sup> Fungi can inhabit water distribution systems, including those of hospitals,<sup>63,64</sup> and may cause nosocomial infection.<sup>51,52</sup> The water system of one hospital in Houston, Tex, harbored *Fusarium* species, causing infections among its patients.<sup>51</sup> Other opportunistic molds, including *Aspergillus* species, have been recovered from the same hospital and from 2 other hospital water systems in Little Rock, Ark.<sup>64</sup> *Exophiala jeanselmei* was responsible for 23 life-threatening nosocomial infections.<sup>52</sup> Additional evidence<sup>65-68</sup> that the opportunistic molds are waterborne comes from the serious infections caused by *Aspergillus* species and *Pseudallescheria boydii* after near-drowning incidents in otherwise healthy individuals. *Pneumocystis carinii* DNA has been recovered from water.<sup>69</sup> Whether *P carinii* exists within hospital water distribution systems needs to be determined in light of the study<sup>70</sup> results suggesting nosocomial transmission of pneumocystosis.

**Parasites.** Outbreaks of toxoplasmosis have been traced to contaminated water<sup>71</sup>; thus, *Toxoplasma gondii* could also potentially cause nosocomial waterborne infections.

**Viruses.** Several pathogenic viruses can also be recovered from water supplies,<sup>8</sup> although nosocomial waterborne infections with these agents have not been reported.

### OUTBREAKS SUPPORTED BY QUALITY EVIDENCE, INCLUDING MOLECULAR RELATEDNESS STUDIES

Some of the older studies\* included in our review did not use the appropriate epidemiologic methods or the modern molecular relatedness tools and relied on weakly discriminatory methods for strain typing, such as serotyping and antibiotic susceptibility patterns (Table 2). However, 29 recent studies† present solid evidence, both epidemiologic and molecular, incriminating the hospital water system as the source of serious waterborne nosocomial infections (Table 1).

The outbreaks mentioned herein probably represent only a subset of the total number of waterborne nosocomial infections because these outbreaks are limited to reports in which the pathogen involved was recovered from the water supply. However, the water supply could also have been the reservoir for pathogens in other out-

\*References 16, 22, 27, 29-31, 33-36, 38-40, 43.

†References 11-15, 17-21, 23-26, 28, 32, 37, 41, 42, 44-52.

**Table 1. Nosocomial Infections Related to the Hospital Water Supply (Tap Water and Water Reservoirs Only): Reports With Supporting Molecular Relatedness Studies\***

Organism	Source	Site(s) of Infection	Method(s) Used to Link Patient and Environmental Strain	Susceptibility of Organism†
<b>Bacteria</b>				
<i>Pseudomonas aeruginosa</i>	Trautmann et al, <sup>11</sup> 2001	Blood, lungs, peritoneum, trachea, urine	AP-PCR	Not reported
	Bert et al, <sup>12</sup> 1998	Lung, sinuses, urine	DNA macrorestriction analysis	Resistant
	Buttery et al, <sup>13</sup> 1998	Blood, central venous catheter, skin, urine	PFGE	Resistant
	Ferroni et al, <sup>14</sup> 1998	Urine	PFGE	Not reported
	Ezpeleta et al, <sup>15</sup> 1998	Blood	ERIC-PCR, RAPD	Not reported
	Burucoa et al, <sup>17</sup> 1995	Not reported	DNA fingerprinting	Susceptible
	Richard et al, <sup>18</sup> 1994	Blood, lung, wound	DNA typing, serotyping	Resistant
	Kolmos et al, <sup>19</sup> 1993	Blood	Phage typing, serogrouping	Susceptible
	Grundmann et al, <sup>20</sup> 1993	Blood, CSF, trachea	Genotyping, serotyping	Not reported
	Worlitzsch et al, <sup>21</sup> 1989	Urine	ExoA DNA probe	Not reported
<i>Stenotrophomonas maltophilia</i>	Weber et al, <sup>23</sup> 1999	Peritoneum, respiratory tract, skin	PFGE	Resistant
	Verweij et al, <sup>24</sup> 1998	Trachea	RAPD	Resistant
	Chachaty et al, <sup>25</sup> 1998	Blood, stools	PFGE	Resistant
	Talon et al, <sup>26</sup> 1994	Blood, stools, throat, urine	PFGE	Resistant
<i>Serratia marcescens</i>	Carlyn et al, <sup>28</sup> 1998	Eye, stools	PFGE	Not reported
<i>Acinetobacter baumannii</i>	Pina et al, <sup>32</sup> 1998	Skin, wound	PFGE, biotyping	Not reported
<i>Aeromonas hydrophila</i>	Picard and Goullet, <sup>37</sup> 1987	Blood	Electrophoretic esterase typing	Not reported
<i>Chryseobacterium</i> species	De Schuijmer et al, <sup>41</sup> 1998	Blood	AP-PCR	Not reported
<b>Mycobacteria</b>				
<i>Mycobacterium avium</i>	Von Reyn et al, <sup>42</sup> 1994	Disseminated	PFGE	Not reported
<i>Mycobacterium fortuitum</i>	Kauppinen et al, <sup>44</sup> 1999	Disseminated	AP-PCR	Susceptible
	Hector et al, <sup>45</sup> 1992	Respiratory tract, wound	PFGE	Not reported
	Burns et al, <sup>46</sup> 1991	Sputum	Phenotype analysis, plasmid profiles, PFGE	Partially reported
<i>Mycobacterium xenopi</i>	Benitez et al, <sup>47</sup> 1999	Various	PCR-based techniques	Not reported
	Desplaces et al, <sup>48</sup> 1995	Spine	Chromosomal restriction fragment patterns	Resistant
<i>Mycobacterium kansasii</i>	Picardeau et al, <sup>49</sup> 1997	Abscess, blood, bone, sputum, stomach, urine	RFLP, PFGE, AFLP, PCR	Not reported
<i>Mycobacterium chelonae</i> and <i>Mycobacterium fortuitum</i>	Wallace et al, <sup>50</sup> 1989	Sternal wound infection, prosthetic valve, Sternal wound infection	Electrophoresis of enzymes, plasmid profiling	Resistant to doxycycline Susceptible to doxycycline
<b>Fungi</b>				
<i>Fusarium solani</i>	Anaissie, <sup>51</sup> 1998	Disseminated	RFLP, RAPD, IR-PCR	Resistant
<i>Exophiala jeanselmei</i>	Nucci et al, <sup>52</sup> 1998	Disseminated	RAPD	Not reported
<i>Aspergillus fumigatus</i>	Anaissie et al, <sup>62</sup> 2002	Lungs	PCR, SSDP	Not reported

\*AP-PCR indicates arbitrarily primed polymerase chain reaction; PFGE, pulse-field gel electrophoresis; ERIC-PCR, enterobacterial repetitive intergenic consensus sequence PCR; RAPD, random amplified polymorphic DNA; CSF, cerebrospinal fluid; ExoA, exotoxin A; RFLP, restriction fragment length polymorphism; AFLP, amplified fragment length polymorphism; IR-PCR, inter-repeat PCR; and SSDP, sequence-specific DNA primer analysis.

†Resistant means resistant to 2 or more classes of antibiotics.

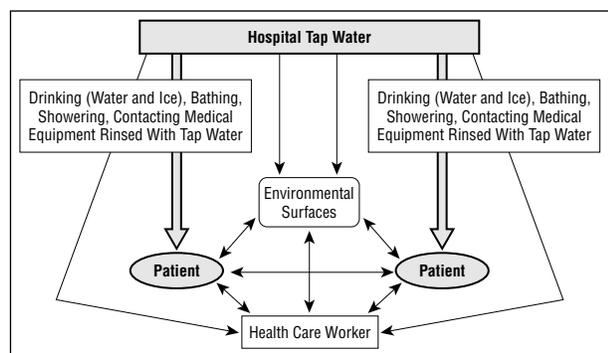
breaks in which cultures of the water supply were not obtained or did not yield the pathogen because of inadequate sampling or variations of the pathogen's load in the water system (related to external factors such as status of the plumbing system and recent obstruction of flow). In such settings, hospital water may have contaminated environmental surfaces (eg, sinks, drains, and whirlpool baths), medical equipment (eg, by rinsing tube feed bags, endoscopes, respiratory equipment, etc, with tap water), or health care providers, leading ultimately to patient exposure<sup>7,72-119</sup> (Figure). Thus, the environmental surfaces, medical equipment, or health care workers may seem to be the pathogen's source; however, hospital water was the primary reservoir but was not tested or the organism was not recovered because of the variables mentioned previously. Forty-nine reported out-

breaks<sup>7,72-119</sup> in which such a scenario could have occurred include infections with the following pathogens: *Acinetobacter baumannii*, *Acinetobacter calcoaceticus*, *Alcaligenes faecalis*, *Alcaligenes xylosoxidans*, *Burkholderia cepacia*, *Enterobacter cloacae*, *Ewingella americana*, *Flavobacterium* species, group A streptococci, *Pseudomonas aeruginosa*, *Serratia marcescens*, *S. maltophilia*, *Pseudomonas thomassii*, *Pseudomonas* species, *Rahnella aquatilis*, *Salmonella urbana*, vancomycin-resistant enterococci, *Mycobacterium chelonae*, *Candida tropicalis*, *Aspergillus niger*, *Acremonium kiliense*, and *Cryptosporidium* species. However, because of the difficulty in identifying the original source of the infection in such reports, we elected to exclude these outbreaks and to limit our review to instances in which the hospital water was clearly documented to be the pathogen's reservoir.

**Table 2. Nosocomial Infections Related to the Hospital Water Supply (Tap Water and Water Reservoirs Only): Reports Without Supporting Molecular Relatedness Studies**

Organism	Source	Site(s) of Infection	Method(s) Used to Link Patient and Environmental Strain	Susceptibility of Organism*
<b>Bacteria</b>				
<i>Pseudomonas aeruginosa</i>	Rudnick et al, <sup>16</sup> 1996	Blood	Serotyping	Not reported
	Martino et al, <sup>22</sup> 1985	Blood	Serotyping	Resistant
<i>Stenotrophomonas maltophilia</i>	Khardori et al, <sup>27</sup> 1990	Blood, lungs, urine, wound	Serotyping, antibiogram	Resistant
<i>Pseudomonas multivorans</i> ( <i>Burkholderia cepacia</i> )	Basset et al, <sup>29</sup> 1970	Wound	Serotyping, antibiogram	Not reported
<i>Pseudomonas mesophilica</i>	Gilchrist et al, <sup>30</sup> 1986	Blood, nasopharynx	Antibiogram	Resistant
<i>Pseudomonas paucimobilis</i>	Crane et al, <sup>31</sup> 1981	Sputum, urine	Temporal association	Not reported
<i>Acinetobacter baumannii</i>	Ritter et al, <sup>33</sup> 1993	Catheter, trachea, stomach, umbilicus	Biochemical profile, antibiogram	Resistant
<i>Enterobacter cloacae</i>	Banjeree et al, <sup>34</sup> 1996	Blood, respiratory tract, urine, wound	Antibiogram	Resistant
<i>Flavobacterium meningosepticum</i>	Pokrywka et al, <sup>35</sup> 1993	Blood, respiratory tract	Temporal association	Susceptible
	Abrahamsen et al, <sup>36</sup> 1989	Blood, meninges	Temporal association	Susceptible
<i>Campylobacter jejuni</i>	Rautelin et al, <sup>38</sup> 1990	Stools	Temporal association	Not reported
<i>Serratia marcescens</i> , <i>Klebsiella oxytoca</i> , <i>Klebsiella pneumoniae</i>	Pegues et al, <sup>40</sup> 1994	Blood, meninges	Serotyping, temporal association	Resistant
<i>P aeruginosa</i> , <i>Pseudomonas vesicularis</i> , <i>S maltophilia</i>	Vanholder et al, <sup>39</sup> 1990	Blood	Temporal association	Not reported
<b>Mycobacteria</b>				
<i>Mycobacterium chelonae</i> subsp <i>abscessus</i>	Soto et al, <sup>43</sup> 1991	Nasal cellulitis	Temporal association	Susceptible

\*Resistant means resistant to 2 or more classes of antibiotics.



Transmission of waterborne pathogens in the hospital setting. Thick arrows indicate routes of transmission that are the subject of this review; thin arrows, other possible routes of transmission that are not included in this review.

### MAGNITUDE OF THE PROBLEM

Although it may be difficult to accurately measure the magnitude of the problem of nosocomial waterborne infections, an estimation of the minimal incidence of these infections and their attributable consequences is possible by focusing on pneumonia with *P aeruginosa* only.

Nosocomial pneumonias account for 20% to 45% of all nosocomial infections<sup>120,121</sup> and for 23 000 deaths per year in the United States alone (1993 data), and 20% of these pneumonias are caused by *P aeruginosa*.<sup>121</sup> Water was confirmed as the source of 10 *P aeruginosa* nosocomial outbreaks in the studies that included molecular relatedness (Table 1), suggesting that outbreaks of nosocomial *P aeruginosa* infections are frequently related to water sources. Indeed, Trautmann et al<sup>11</sup> found in a 7-month prospective study at a surgical intensive care ward that 5 (29%) of 17 patients were infected with *P aeruginosa* genotypes

detectable in tap water. Despite an extensive literature search, we did not find studies (that included molecular relatedness studies) that linked nosocomial *P aeruginosa* infections with other accepted hospital sources for *P aeruginosa*, such as fruits, vegetables, and plants.

Because 20% of nosocomial pneumonias are caused by *P aeruginosa*,<sup>121</sup> for an estimated 4600 deaths per year, and because 30% of these infections are waterborne,<sup>11</sup> the annual mortality from waterborne *P aeruginosa* nosocomial pneumonia in the United States is approximately 1400. This estimate is conservative considering that several other waterborne pathogens can also be responsible for nosocomial pneumonia (Tables 1 and 2), that these pathogens may cause a variety of other infections (Tables 1 and 2), and that such waterborne infections are frequently underdiagnosed<sup>122</sup> or missed for several years.<sup>123-125</sup> Thus, the effect of waterborne pathogens in the hospital setting may be enormous.

### MODE OF TRANSMISSION TO PATIENTS

The primary cause of diminished water quality is the buildup of biofilm and the corrosion of distribution lines and tank surfaces resulting from poor design or aging of distribution systems and water stagnation.<sup>55,126</sup> Increased water demand during summer or when construction activity increases flow through stagnant pipelines, dislodging organisms from biofilms and releasing them into the water supply.<sup>55,57</sup>

Patient exposure to waterborne microorganisms in the hospital occurs while showering, bathing, and drinking (water or ice)<sup>127-129</sup> and through contact with contaminated medical equipment (eg, tube feed bags, endoscopes, and respiratory equipment) rinsed with tap water.<sup>7,12</sup> The sources of organisms include hospital water tanks, fau-

**Table 3. Public Health Agency Guidelines Regarding Community and Hospital Water Precautions**

Agency	Community Setting	Hospital Setting
United Kingdom Departments of the Environment and Health	Sterile water <sup>133</sup>	Not applicable
United States Centers for Disease Control and Prevention Other agencies and associations*	Educate patients about (1) risk of acquiring infections from tap water and (2) avoidance of tap water	Prevention of pneumonia <sup>136</sup> and opportunistic infections in hematopoietic stem cell transplant recipients <sup>137</sup> <i>Legionella</i> Routinely maintain the hospital water supply Avoid tap water exposure and provide sterile water for drinking to high-risk patients if <i>Legionella</i> species are detected in the water supply <i>Aspergillus</i> species and other fungi Formulate hospital policies to minimize exposure of high-risk patients to sources of <i>Aspergillus</i> species Eliminate exposure to activities that may aerosolize fungi Eliminate hospital sources of fungi if found Promptly clean and repair water leaks to prevent mold proliferation in patient care areas

\*Environmental Protection Agency, Food and Drug Administration, National Institutes of Health, American Society for Microbiology, Society of Healthcare Epidemiologists of America, Department of Agriculture, Infectious Disease Society of America, American Public Health Association, American Society of Tropical Medicine and Hygiene, American Water Works Association, Water Quality Association, Association of Metropolitan Water Agencies, Association of State and Territorial Public Health Laboratory Directors, American Dental Association, American Dietetic Association, National Alliance of State and Territorial AIDS Directors, National Association of County Health Officials, National Association of Persons With AIDS, National Association of State Public Health Veterinarians, National Center for Infectious Diseases, National Institute of Allergy and Infectious Diseases, and Council of State and Territorial Epidemiologists.

cet tap water, and showers. Even small quantities of organisms in water can cause infection<sup>66-68,126-129,130</sup>; 1 oocyst of *Cryptosporidium parvum* per 1000 L of drinking water could result in 6000 infections per year in a city the size of New York,<sup>131</sup> and a single exposure to 200 mL of water may result in serious mold infections.<sup>66-69,130</sup>

Only one<sup>20</sup> of the studies evaluated the hospital water supply for the presence of this pathogen and did not find it. The absence of this organism in the water supply does not by itself rule out the fact that the system was contaminated. Potential explanations include the limited number of samples obtained in the study and the contamination of a segment of the system only. It is possible, however, that contamination of the faucets by patients may have occurred.

#### CURRENT PREVENTIVE GUIDELINES

##### Community Guidelines for the Prevention of Waterborne Infections

After the 1993 outbreak of cryptosporidiosis in Milwaukee, Wis (403 000 infections, 4400 hospitalizations, and 104 deaths),<sup>132</sup> several public health agencies issued recommendations that targeted immunodepressed patients.<sup>133,134</sup> These recommendations stated that such patients “should be provided information about measures to ensure their drinking water is safe” and should “only drink water that is bottled sterile, submicron filtered or boiled, in outbreak settings.”<sup>134</sup> After the outbreaks of cryptosporidiosis, the Departments of the Environment and Health<sup>133</sup> of the United Kingdom issued even stricter recommendations that “people with impaired immunity should not drink unboiled water.” Additional US government-mandated water purity standards for the prevention of community-acquired infections were re-

cently announced under amendments to the Safe Drinking Water Act.<sup>135</sup>

##### Hospital Guidelines for the Prevention of Legionellosis and Aspergillosis

The Centers for Disease Control and Prevention (CDC), Atlanta, Ga, developed recommendations for the prevention of nosocomial pneumonia and legionellosis that include routine maintenance of the hospital water supply system and consideration for the use of sterile water in immunodepressed patients.<sup>136</sup> For the prevention of hospital-acquired aspergillosis,<sup>136</sup> the CDC “strongly recommends” the following: (1) minimizing exposure of high-risk patients to potential sources of *Aspergillus* species and to activities that may aerosolize *Aspergillus* and other fungi and (2) eliminating the source of aspergilli. Because opportunistic molds can inhabit hospital water systems and aerosolize after water activities,<sup>63,64</sup> these CDC recommendations imply that water precautions need to be introduced in hospitals caring for patients at risk for opportunistic mycoses. Because the data on the potential waterborne nature of nosocomial aspergillosis were not available at the time of these recommendations, specific recommendations to avoid water exposure to prevent aspergillosis were not offered.<sup>136</sup>

Finally, when the hospital water of institutions caring for stem cell transplant recipients is colonized with *Legionella* species, the CDC recommends the use of sterile water for drinking, brushing teeth, flushing nasogastric tubes, and rinsing nebulization devices and other semicritical respiratory care equipment. The CDC also recommends avoiding showering (using sponge baths instead) and exposure to faucet water and prompt cleaning and repair of water leaks to prevent mold proliferation in patient care areas (**Table 3**).<sup>137</sup>

**Table 4. Effective Measures Used to Terminate Outbreaks of Nosocomial Waterborne Infections**

Method	Source
Repair of water systems	Banjeree et al, <sup>34</sup> 1996
Disinfection of water distribution systems, including tanks	Chachaty et al, <sup>25</sup> 1998; Picard and Gouillet, <sup>37</sup> 1987; Vanholder et al, <sup>39</sup> 1990; Soto et al, <sup>43</sup> 1991
Maintenance program	
Entire water system	Chachaty et al, <sup>25</sup> 1998; Picard and Gouillet, <sup>37</sup> 1987; Vanholder et al, <sup>39</sup> 1990
Monitoring of faucet taps	Ferroni et al, <sup>14</sup> 1998; Kolmos et al, <sup>19</sup> 1993
Avoidance of tap water (for bathing, drinking, and procedures)	Verweij et al, <sup>24</sup> 1998; Chachaty et al, <sup>25</sup> 1998; Picard and Gouillet, <sup>37</sup> 1987; Breiman et al, <sup>127</sup> 1990
Restriction of connection of equipment to water sources until immediately before use	Rudnick et al, <sup>16</sup> 1996; Kolmos et al, <sup>19</sup> 1993

**Table 5. Efficacy of Water Disinfection Methods Against Various Pathogens\***

Method	<i>Legionella</i>	Mycobacteria	Molds	Viruses	Parasites
Distillation or boiling	Excellent	Excellent	Excellent	Excellent	Excellent
Chlorination	Fair-good	Poor	Poor	Good	Poor
Reverse osmosis	Good	Good	Not tested	Good	Excellent
Copper/silver ionization	Excellent†	Not tested	Not tested	Not tested	Not tested
Submicron filtration	NA	Not tested	Not tested‡	Poor	Excellent
Ozonation	Good	Not tested	Not tested	Excellent	Excellent
UV irradiation	Good	Not tested	Not tested	Fair-poor	Excellent
Iodinated resin	Good	Poor	Not tested	Good	Poor

\*Excellent indicates eliminates all microbes (highly effective); good, clinically significant reduction in microbial load; fair, some reduction in microbial load but questionable clinical relevance; and poor, little or no effect on microbial load (not clinically useful).

†Limited experience.  
‡Likely to be effective.

## RECOMMENDATIONS FOR PREVENTING NOSOCOMIAL WATERBORNE INFECTIONS

Government agencies have established guidelines for water safety in the community, particularly for immunocompromised persons.<sup>133,134</sup> Given the greater vulnerability of these patients to infection when hospitalized (usually at the peak of their immunosuppression), hospitals caring for such patients should provide higher standards of drinking water quality than the community and should take immediate measures to prevent waterborne infections. These measures are likely to be successful, as demonstrated by the significant reduction in waterborne infections (such as legionellosis and cryptosporidiosis) when guidelines are applied.<sup>129,138</sup>

To this end, we offer the single new recommendation of minimizing patient exposure to tap water for all hospitalized immunocompromised patients and reinforce previously published recommendations, ie, to educate staff and patients, implement existing infection control measures, and perform targeted surveillance.

### I. Minimize Patient Exposure to Tap Water: Inexpensive Yet Potentially Effective

This measure is the easiest and least expensive to implement. Its effectiveness has been demonstrated by studies in which provision of sterile water or avoidance of tap water markedly reduced the incidence of legionellosis<sup>129</sup> and cryptosporidiosis<sup>138</sup> and terminated several other outbreaks of nosocomial waterborne infections (**Table 4**).

We recommend implementation of the CDC guidelines<sup>136,137</sup> regardless of the colonization of hospital water systems by *Legionella* species. We further recommend expanding these CDC guidelines to all immunocompromised patients. Our recommendations are based on the following: (1) culturing of hospital water for *Legionella* species is not routinely performed at most transplantation centers, as evidenced by the outbreaks of legionellosis on such units, which may go unrecognized for up to 10 years<sup>123-125</sup>; (2) opportunistic molds can inhabit hospital water systems and aerosolize after water activities, leading to patient exposure<sup>63,64</sup>; and (3) other hospitalized immunocompromised patient populations (cancer patients, solid organ transplant recipients, etc) are also at risk for legionellosis<sup>58</sup> and other nosocomial waterborne infections.<sup>11-52</sup> These patient populations should, thus, be offered the same level of protection given to recipients of hematopoietic stem cell transplants.

Sterile water can be produced by vigorous boiling for 3 minutes or can be purchased at a minimal cost (\$0.49/gal average price). Of note, bottled water is not necessarily sterile unless so labeled. Other water disinfection technologies are available, but distillation seems to be the most appropriate approach to producing sterile water in small quantities (**Table 5**). However, extraordinary effort would be required to establish and maintain distillation systems sufficient to provide sterile drinking water to all hospitalized patients. Because of its low cost and worldwide availability, sterile drinking water (obtained by vigorous boiling or purchased as bottled water) should be provided to immunocompromised patients. Because showering is as-

sociated with nosocomial waterborne infections<sup>127</sup> and results in aerosolization of pathogens,<sup>63,64</sup> it would seem prudent to avoid showering and to rely instead on disposable sterile sponges for bathing. These sponges are inexpensive (<\$1.50 per patient per day), require less nursing time in the bathing of patients compared with showering these patients or providing them with the usual self-prepared bed baths, and are well accepted by caregivers.<sup>139</sup> Alternatively, patients may prepare their own sterile sponge bath with towels that have been steamed or microwaved and water that has been boiled. Special care must be taken to avoid serious burns in this setting. Appropriate disinfection of hospital equipment and avoidance of contact of such equipment with tap water is also recommended.<sup>140</sup>

It could be argued that it was failure in infection control practices (such as failure to wash hands) that contributed to some of these waterborne outbreaks and that implementation of effective practices will suffice to prevent these infections. However, a significant rate of nosocomial infections (10%) persisted even after a significant improvement in compliance with hand hygiene (from 48% to 66%).<sup>141</sup> In addition, and despite extensive education about the importance of infection control measures, adherence among health care workers remains low.<sup>141</sup> Thus, a more redundant system needs to be put in place that relies on more than one method to prevent these infections. Provision of sterile water is an inexpensive measure that could provide such redundancy.

It could also be argued that institutions caring for high-risk patients have already undertaken such precautions. Such is not the case, however, as evidenced by the recent reports of outbreaks of legionellosis in transplantation units that went undetected for up to 10 years.<sup>123-125</sup>

## II. Educate Staff and Patients and Implement Existing Infection Control Measures

Hospital staff members and patients should receive education about the procedures that prevent infection from waterborne pathogens in hospital and outpatient settings (per US and United Kingdom public health agencies).<sup>133,134</sup> Reinforcement of infection control measures that have ended outbreaks in the past is also needed. These measures include hand disinfection, use of other aseptic techniques, discontinuation of the use of contaminated equipment, restriction of equipment connection to water sources until immediately before use, effective instrument sterilization, and meticulous disinfection of the ward environment (Table 4).

## III. Perform Targeted Surveillance

Two approaches for the control of nosocomial legionellosis have been recommended: (1) intensive surveillance for infections and monitoring of water systems when infections occur<sup>142</sup> and (2) routine surveillance cultures of water distribution systems in hospitals caring for high-risk patients.<sup>143</sup>

Although we favor the latter approach in the case of legionellosis, we believe that intensive surveillance for infections other than by *Legionella* species is more appropriate until the extent of the relationship between in-

fection and water colonization by these pathogens has been established. Such surveillance, however, should be intensive, comprehensive of all hospital wards, and prolonged and should rely on appropriate tools to diagnose these infections and their relation to the water source.

## IV. Other Measures

One potentially effective approach is to maintain hot water at 60°C or higher<sup>140</sup> in an attempt to decrease the concentration of organisms in hospital water systems. However, we do not view this approach as particularly appealing because of the considerable costs, the short-term effectiveness of this measure, and the risk of accidental scalding injury of patients and staff.

New hospitals should construct water distribution systems that meet the American Institute of Architects specifications,<sup>140</sup> and, per CDC and Association for Professionals in Infection Control and Epidemiology recommendations, all hospitals should conduct routine preventive maintenance of their water distribution system. Unlike residential water tanks, which are based on flow-through systems, large buildings such as hospitals are required to have recirculating hot water systems, which are associated with a significant increase in risk of colonization by and amplification of these pathogens.<sup>8</sup> Water filtration systems are not consistently effective, are expensive, and are difficult to maintain.<sup>144</sup> Thus, physical barriers (avoidance of exposure) remain the best forms of protection. This conclusion is supported by the lower cost, ease of implementation, and effectiveness of such measures compared with the high cost, complexity, and limited success of disinfection methods (waterborne organisms rapidly recolonize water structures).<sup>145</sup> Important measures to decrease the concentration of organisms present in hospital water systems consist of repairing and disinfecting damaged and contaminated water systems (including tanks) and establishing a regular maintenance program (Table 4).

## CONCLUSIONS

The literature demonstrates a strong association between waterborne pathogens and nosocomial infections other than legionellosis. This association is not well appreciated and is still not fully understood. The most rigorous approach to better understanding the magnitude of the problem is the conduct of carefully planned prospective studies. These studies should prospectively assess the magnitude of the problem of nosocomial waterborne infections and the percentage of hospitals that have microbial contamination of their water supply. These studies should also attempt to correlate rates of nosocomial pneumonia with counts of waterborne gram-negative organisms such as *P aeruginosa* and with certain hospital practices such as superheating and flushing or other control methods for waterborne legionellosis.

This review does not demonstrate that instituting our new recommendation of avoiding patient exposure to tap water would result in a decreased incidence of all waterborne nosocomial infections. However, the effectiveness of this easy, inexpensive, and readily and widely available approach has been demonstrated by studies in which provision of ster-

ile water or avoidance of tap water markedly reduced the incidence of waterborne infections, including legionellosis<sup>129</sup> and cryptosporidiosis,<sup>138</sup> and terminated several other outbreaks of nosocomial waterborne infections (Table 4).\*

Accepted for publication November 15, 2001.

This study was presented in part at the 38th Interscience Conference for Antimicrobial Agents and Chemotherapy, San Diego, Calif, September 27, 1998.

We thank Robert Bradsher, MD, J. Peter Donnelly, PhD, Thomas Marrie, MD, Janet Stout, PhD, and Robert Rubin, MD, for their insight and critical review of the manuscript.

Corresponding author: Elias J. Anaissie, MD, Myeloma and Transplantation Research Center, University of Arkansas for Medical Sciences, 4301 W Markham, Mail Slot 776, Little Rock, AR 72205 (e-mail: anaissieeliasj@uams.edu or elias114@aol.com).

## REFERENCES

- Pittet D. Nosocomial bloodstream infections. In: Wenzel RP, ed. *Prevention and Control of Nosocomial Infections*. Baltimore, Md: Williams & Wilkins; 1997: 711-769.
- Rex JH, Sobel JD. Preventing intra-abdominal infections in surgical patients. *Crit Care Med*. 1999;27:1033-1034.
- Emori TG, Gaynes RP. An overview of nosocomial infections, including the role of the microbiology laboratory. *Clin Microbiol Rev*. 1993;6:428-442.
- Weber DJ, Raasch R, Rutala WA. Nosocomial infections in the ICU: the growing importance of antibiotic-resistant pathogens. *Chest*. 1999;115(suppl):34S-41S.
- Pfaller MA, Herwaldt LA. The clinical microbiology laboratory and infection control: emerging pathogens, antimicrobial resistance, and new technology. *Clin Infect Dis*. 1997;25:858-870.
- Rex JH, Walsh TJ, Anaissie EJ. Fungal infections in iatrogenically compromised hosts. *Adv Intern Med*. 1998;43:321-371.
- Rutala W, Weber D. Water as a reservoir of nosocomial pathogens. *Infect Control Hosp Epidemiol*. 1997;18:609-616.
- Geldreich EE. Creating microbial quality in drinking water. In: Geldreich EE, ed. *Microbial Qualities of Water Supply in Distribution Systems*. Boca Raton, Fla: CRC Press Inc; 1996:39-102.
- Yu V, Liu Z, Stout JE, Goetz A. *Legionella* disinfection of water distribution systems: principles, problems, and practice. *Infect Control Hosp Epidemiol*. 1993; 14:571-575.
- Moffet HL, Williams T. Bacteria recovered from distilled water and inhalation therapy equipment. *AJDC*. 1967;114:7-12.
- Trautmann M, Michalsky T, Heidemarie W, Radosavljevic V, Ruhnke M. Tap water colonization with *Pseudomonas aeruginosa* in a surgical intensive care unit (ICU) and relation to *Pseudomonas* infections of ICU patients. *Infect Control Hosp Epidemiol*. 2001;22:49-52.
- Bert F, Maubec E, Bruneau B, Berry P, Lambert-Zechovsky N. Multi-resistant *Pseudomonas aeruginosa* outbreak associated with contaminated tap water in a neurosurgery intensive care unit. *J Hosp Infect*. 1998;39:53-62.
- Buttery JP, Alabaster SJ, Heine RG, Scott SM, Crutchfield RA, Garland SM. Multiresistant *Pseudomonas aeruginosa* outbreak in a pediatric oncology ward related to bath toys. *Pediatr Infect Dis J*. 1998;17:509-513.
- Ferroni A, Nguyen B, Pron B, Quesne G, Brusset MC, Berche P. Outbreak of nosocomial urinary tract infections due to *Pseudomonas aeruginosa* in a pediatric surgical unit associated with tap-water contamination. *J Hosp Infect*. 1998; 39:301-307.
- Ezpeleta C, Larrea I, Martinez J, Arrese E, Cisterna R. *Pseudomonas aeruginosa* bacteremia following ERCP: an investigation of sources by molecular typing methods. In: Program and abstracts of the 38th Interscience Conference on Antimicrobial Agents and Chemotherapy; September 24-27, 1998; San Diego, Calif. Abstract K-73.
- Rudnick J, Beck-Sague CM, Anderson RL, Schable B, Miller JM, Jarvis WR. Gram-negative bacteremia in open-heart surgery patients traced to potable tap-water contamination of pressure-monitoring equipment. *Infect Control Hosp Epidemiol*. 1996;17:281-285.
- Burucoa C, Lhomme V, Gorin V, et al. Water-borne hospital outbreak due to *Pseudomonas aeruginosa*. In: Program and abstracts of the 35th Interscience Conference on Antimicrobial Agents and Chemotherapy; September 17-20, 1995; San Francisco, Calif. Abstract J-126.
- Richard P, Le Floch R, Chamoux C, Pannier M, Espaze E, Richet H. *Pseudomonas aeruginosa* outbreak in a burn unit: role of antimicrobials in the emergence of multiply resistant strains. *J Infect Dis*. 1994;170:377-383.
- Kolmos HJ, Thuesen B, Nielsen SV, Lohmann M, Kristoffersen K, Rosdahl VT. Outbreak of infection in a burn unit due to *Pseudomonas aeruginosa* originating from contaminated tubing used for irrigation of patients. *J Hosp Infect*. 1993; 4:11-21.
- Grundmann H, Kropec A, Hartung D, Berner R, Daschner F. *Pseudomonas aeruginosa* in a neonatal intensive care unit: reservoirs and ecology of the nosocomial pathogen. *J Infect Dis*. 1993;168:943-947.
- Worlitzsch D, Wolz C, Botzenhart K, et al. Molecular epidemiology of *Pseudomonas aeruginosa*: urinary tract infections in paraplegic patients. *Zentralbl Hyg Umweltmed*. 1989;189:175-184.
- Martino P, Venditti M, Papa G, Orefici G, Serra P. Water supply as a source of *Pseudomonas aeruginosa* in a hospital for hematological malignancies. *Boll Ist Sieroter Milan*. 1985;64:109-114.
- Weber DJ, Rutala WA, Blanchet CN, Jordan M, Gergen MF. Faucet aerators: a source of patient colonization with *Stenotrophomonas maltophilia*. *Am J Infect Control*. 1999;27:59-63.
- Verweij PE, Meis JF, Christmann V, et al. Nosocomial outbreak of colonization and infection with *Stenotrophomonas maltophilia* in preterm infants associated with contaminated tap water. *Epidemiol Infect*. 1998;120:251-256.
- Chachaty E, Castagna L, Massei B, et al. Outbreak of *Stenotrophomonas maltophilia* infections in neutropenic patients: role of water distribution in hospital. In: Program and abstracts of the 38th Interscience Conference on Antimicrobial Agents and Chemotherapy; September 24-27, 1998; San Diego, Calif. Abstract K-74.
- Talon D, Bailly P, Leprat R, et al. Typing of hospital strains of *Xanthomonas maltophilia* by pulsed-field gel electrophoresis. *J Hosp Infect*. 1994;27:209-217.
- Khadori N, Elting L, Wong E, Schable B, Bodey GP. Nosocomial infections due to *Xanthomonas maltophilia* (*Pseudomonas maltophilia*) in patients with cancer. *Rev Infect Dis*. 1990;12:997-1003.
- Carlyn C, Simmonds J, Kondracki S, et al. An outbreak of *Serratia marcescens* conjunctivitis in a neonatal care unit: genotypic link to an environmental source. In: Program and abstracts of the 8th Annual Meeting of the Society for Healthcare Epidemiology of America; April 5-7, 1998; Orlando, Fla. Abstract 1998: Oral 116.
- Basset D, Stokes KJ, Thomas WRG. Wound infections with *Pseudomonas multivorans*: waterborne contaminant of disinfectant solutions. *Lancet*. 1970;1: 1188-1191.
- Gilchrist MJ, Kraft JA, Hammond JG, Connelly BL, Myers MG. Detection of *Pseudomonas mesophilica* as a source of nosocomial infections in a bone marrow transplant unit. *J Clin Microbiol*. 1986;23:1052-1055.
- Crane LR, Tagle LC, Palutke WA. Outbreak of *Pseudomonas paucimobilis* in an intensive care nursery. *JAMA*. 1981;246:985-987.
- Pina P, Guezenc P, Grosbuis S, Guyot L, Ghnassia JC, Allouch PY. An *Acinetobacter baumannii* outbreak at the Versailles Hospital Center. *Pathol Biol (Paris)*. 1998;46:385-394.
- Ritter E, Thurm V, Becker-Boost E, Thomas P, Finger H, Wirsing von Konig CH. Epidemic occurrences of multiresistant *Acinetobacter baumannii* strains in a neonatal intensive care unit. *Zentralbl Hyg Umweltmed*. 1993;193:461-470.
- Banjeree G, Ayyagari A, Prasad KN, Dhole TN, Singh SK. Nosocomial infection due to *Enterobacter cloacae* in a tertiary care hospital in Northern India. *Indian J Med Res*. 1996;103:58-61.
- Pokrywka M, Viazanko K, Medvick J, et al. A *Flavobacterium meningosepticum* outbreak among intensive care patients. *Am J Infect Control*. 1993;17:139-145.
- Abrahamson TG, Finne PH, Lingaas E. *Flavobacterium meningosepticum* infections in a neonatal intensive care unit. *Acta Paediatr Scand*. 1989;78:51-55.
- Picard B, Goulet P. Epidemiological complexity of hospital *Aeromonas* infections revealed by electrophoretic typing of esterases. *Epidemiol Infect*. 1987; 98:5-14.
- Rautelin H, Koota K, von Essen R, Jahkola M, Siitonen A, Kosunen TU. Waterborne *Campylobacter jejuni* epidemic in a Finnish hospital for rheumatic diseases. *Scand J Infect Dis*. 1990;22:321-326.
- Vanholder R, Vanhaecke E, Ringoir S. Waterborne *Pseudomonas* septicemia. *ASAIO Trans*. 1990;36:M215-M216.
- Pegues DA, Arathoon EG, Samayoa B, et al. Epidemic gram-negative bacteremia in a neonatal intensive care unit in Guatemala. *Am J Infect Control*. 1994; 22:163-171.
- De Schuijmer J, Vammeste M, Vannechoutte M, Verschraegen G. *Chryseobacterium* in a burn unit. In: Program and abstracts of the 4th International Conference of the Hospital Infection Society; September 13-17, 1998; Edinburgh, Scotland.

\*References 12, 14, 16, 19, 24, 25, 31, 32, 34, 36, 37, 39, 43, 48.

42. Von Reyn C, Maslow JN, Barber TW, Falkinham JO III, Arbeit RD. Persistent colonisation of potable water as a source of *Mycobacterium avium* infection in AIDS. *Lancet*. 1994;343:1137-1141.
43. Soto LE, Bobadilla M, Villalobos Y, et al. Post-surgical nasal cellulitis outbreak due to *Mycobacterium chelonae*. *J Hosp Infect*. 1991;19:99-106.
44. Kauppinen J, Nousiainen T, Jantunen E, Mattila R, Katila ML. Hospital water supply as a source of disseminated *Mycobacterium fortuitum* infection in a leukemia patient. *Infect Control Hosp Epidemiol*. 1999;20:343-345.
45. Hector JS, Pang Y, Mazurek GH, Zhang Y, Brown BA, Wallace RJ Jr. Large restriction fragment patterns of genomic *Mycobacterium fortuitum* DNA as strain-specific markers and their use in epidemiologic investigation of four nosocomial outbreaks. *J Clin Microbiol*. 1992;30:1250-1255.
46. Burns DN, Wallace RJ, Schultz ME, et al. Nosocomial outbreak of respiratory tract colonization with *Mycobacterium fortuitum*: demonstration of the usefulness of pulsed-field gel electrophoresis in an epidemiologic investigation. *Am Rev Respir Dis*. 1991;144:1153-1159.
47. Benitez MA, Alcaide F, Rufi G, Sanuy B, Gudiol F, Martin R. Investigation of a nosocomial outbreak of *Mycobacterium xenopi* associated with a hospital water supply. In: Program and abstracts of the 39th Interscience Conference on Antimicrobial Agents and Chemotherapy; September 26-29, 1999; San Diego, Calif. Abstract 753.
48. Desplaces N, Picardeau M, Dinh V, et al. Spinal infections due to *Mycobacterium xenopi* after discectomies. In: Program and abstracts of the 35th Interscience Conference on Antimicrobial Agents and Chemotherapy; September 17-20, 1995; San Francisco, Calif. Abstract J-145.
49. Picardeau M, Prod'Hom G, Raskine L, Le Pennec MP, Vincent V. Genotypic characterization of five subspecies of *Mycobacterium kansasii*. *J Clin Microbiol*. 1997;35:25-32.
50. Wallace RJ, Musser JM, Hull SI, et al. Diversity and sources of rapidly growing mycobacteria associated with infections following cardiac surgery. *J Infect Dis*. 1989;159:708-716.
51. Anaissie E. Emerging fungal infections: don't drink the water. In: Program and abstracts of the 38th Interscience Conference on Antimicrobial Agents and Chemotherapy; September 24-27, 1998; San Diego, Calif. Abstract S-147.
52. Nucci M, Akiti T, Silveira F, et al. Fungemia due to *Exophiala jeanselmei*: report of 23 cases. In: Program and abstracts of the 38th Interscience Conference of Antimicrobial Agents and Chemotherapy; September 24-27, 1998; San Diego, Calif. Abstract J-141.
53. Armstrong JL, Calomiris JJ, Seidler RJ. Selection of antibiotic-resistant standard plate count bacteria during water treatment. *Appl Environ Microbiol*. 1982;44:308-16.
54. Jochimesen EM, Carmichael WW, An JS, et al. Liver failure and death after exposure to microcystins at a hemodialysis center in Brazil. *N Engl J Med*. 1998;26:873-878.
55. Geldreich EE. Biofilms in water distribution system. In: CRC Press Inc, ed. *Microbial Qualities of Water Supply in Distribution Systems*. Boca Raton, Fla: Lewis Publisher; 1996:159-214.
56. Geldreich EE. Biological profiles in drinking water. In: Geldreich EE, ed. *Microbial Qualities of Water Supply in Distribution Systems*. Boca Raton, Fla: CRC Press Inc; 1996:104-144.
57. Mermel L, Josephson SL, Giorgio CH, Dempsey J, Parenteau S. Association of Legionnaire's disease with construction: contamination of potable water? *Infect Control Hosp Epidemiol*. 1995;16:76-81.
58. Yu VL. *Legionella pneumophila* (Legionnaires' disease). In: Mandell DAD, ed. *Principles and Practice of Infectious Diseases*. Vol 2. 5th ed. Philadelphia, Pa: Churchill Livingstone Inc; 2000:2424-2435.
59. Michel R, Burghardt H, Bergmann H. *Acanthamoeba*, naturally intracellularly infected with *Pseudomonas aeruginosa*, after their isolation from a microbiologically contaminated drinking water system in a hospital. *Zentralbl Hyg Umweltmed*. 1995;196:532-544.
60. Walochnik J, Picher O, Aspöck C, Ullman M, Sommer R, Aspöck H. Interactions of "Limax amoebae" and gram-negative bacteria: experimental studies and review of current problems. *Tokai J Exp Clin Med*. 1998;23:273-278.
61. Pannuti CS. Hospital environment for high risk patients. In: Wenzel RP, ed. *Prevention and Control of Nosocomial Infections*. 3rd ed. Baltimore, Md: Williams & Wilkins; 1997:463-489.
62. Anaissie EG, Stratton SL, Dignani MC, et al. Pathogenic *Aspergillus* species recovered from a hospital water system: a 3-year prospective study. *Clin Infect Dis*. 2002;34:780-789.
63. Anaissie E, Kuchar R, Rex J, Summerbell R, Walsh T. The hospital water system as a reservoir of *Fusarium*. In: Program and abstracts of the 37th Interscience Conference on Antimicrobial Agents and Chemotherapy; September 28-October 1, 1997; Toronto, Ontario. Abstract J-94.
64. Anaissie EJ, Monson TP, Penzak SR, Stratton SL. Opportunistic fungi recovered from hospital water systems. In: Program and abstracts of the 37th Interscience Conference on Antimicrobial Agents and Chemotherapy; September 28-October 1, 1997; Toronto, Ontario. Abstract J-93.
65. Anonymous. Air is apparent, but water can also be a source. In: Evans G, ed. *Infection Control Sourcebook*. Atlanta, Ga: American Health Consultants; 1997: E32-E33.
66. Mizukane R, Sawatari K, Araki J, et al. Invasive pulmonary aspergillosis caused by aspiration of polluted water after nearly drowning [in Japanese]. *Kansenshogaku Zasshi*. 1996;70:1181-1185.
67. ter Maaten JC, Golding RP, Strack van Schijndel RJ, Thijs LG. Disseminated aspergillosis after near drowning. *Neth J Med*. 1995;47:21-24.
68. Wilichowski E, Christen HJ, Schiffmann H, Schulz-Schaeffer W, Behrens-Baumann W. Fatal *Pseudallescheria boydii* panencephalitis in a child after nearly drowning. *Pediatr Infect Dis J*. 1996;15:365-370.
69. Casanova L, Leibowitz M. Detection of DNA from *Pneumocystis carinii* in water. In: Program and abstracts of the 37th Interscience Conference of Antimicrobial Agents and Chemotherapy; September 28-October 1, 1997; Toronto, Ontario. Abstract K-116.
70. Gerberding JL. Nosocomial transmission of opportunistic infections. *Infect Control Hosp Epidemiol*. 1998;19:574-577.
71. Bowie WR, King AS, Werker DH, et al, for the BC Toxoplasma Investigation Team. Outbreak of toxoplasmosis associated with municipal drinking water. *Lancet*. 1997;350:173-177.
72. Muyldermans G, de Smet F, Pierard D, et al. Neonatal infections with *Pseudomonas aeruginosa* associated with a water-bath used to thaw fresh frozen plasma. *J Hosp Infect*. 1998;39:309-314.
73. Piper J, Tuttle D, McGrail L, Steele-Moore L, Bollinger E, Berg D. *Pseudomonas aeruginosa* outbreak in a neonatal ICU due to construction related water line alterations. In: Program and abstracts of the 37th Interscience Conference of Antimicrobial Agents and Chemotherapy; September 28-October 1, 1997; Toronto, Ontario. Abstract J-21.
74. De Vos D, Lim A Jr, Pirnay JP, et al. Analysis of epidemic *Pseudomonas aeruginosa* isolates by isoelectric focusing of pyoverdine and RAPD-PCR: modern tools for an integrated anti-nosocomial infection strategy in burn wound centres. *Burns*. 1997;23:379-386.
75. Doring G, Jansen S, Noll H, et al. Distribution and transmission of *Pseudomonas aeruginosa* and *Burkholderia cepacia* in a hospital ward. *Pediatr Pulmonol*. 1996;21:90-100.
76. Kerr JR, Moore JE, Curran MD, et al. Investigation of a nosocomial outbreak of *Pseudomonas aeruginosa* pneumonia in an intensive care unit by random amplification of polymorphic DNA assay. *J Hosp Infect*. 1995;30:125-131.
77. Doring G, Horz M, Ortelt J, Grupp H, Wolz C. Molecular epidemiology of *Pseudomonas aeruginosa* in an intensive care unit. *Epidemiol Infect*. 1993;110:427-436.
78. Tredget EE, Shankowsky HA, Joffe AM, et al. Epidemiology of infections with *Pseudomonas aeruginosa* in burn patients: the role of hydrotherapy. *Clin Infect Dis*. 1992;15:941-949.
79. Casewell MW, Slater NG, Cooper JE. Operating theatre water-baths as a cause of pseudomonas septicemia. *J Hosp Infect*. 1981;2:237-247.
80. Griffith SJ, Nathan C, Selander RK, et al. The epidemiology of *Pseudomonas aeruginosa* in oncology patients in a general hospital. *J Infect Dis*. 1989;160:1030-1036.
81. Schleich WF, Simonsen N, Sumarah R, Martin RS. Nosocomial outbreak of *Pseudomonas aeruginosa* folliculitis associated with a physiotherapy pool. *CMAJ*. 1986;134:909-913.
82. Levin MH, Olson B, Nathan C, Kabins SA, Weinstein RA. *Pseudomonas* in the sinks in an intensive care unit: relation to patients. *J Clin Pathol*. 1984;37:424-427.
83. McGuckin MB, Thorpe RJ, Abrutyn E. Hydrotherapy: an outbreak of *Pseudomonas aeruginosa* wound infections related to Hubbard tank treatments. *Arch Phys Med Rehabil*. 1981;62:283-285.
84. Burdon DW, Whitby JL. Contamination of hospital disinfectants with *Pseudomonas* species. *BMJ*. 1967;2:153-155.
85. Cross DF, Benchimol A, Dimond EG. The faucet aerator: a source of pseudomonas infection. *N Engl J Med*. 1966;274:1430-1431.
86. Kresky B. Control of gram-negative bacilli in a hospital nursery. *AJDC*. 1964;107:363-369.
87. Wilson MG, Nelson RC, Phillips LH, Boak RA. New source of *Pseudomonas aeruginosa* in a nursery. *JAMA*. 1961;175:1146-1148.
88. Villarino ME, Stevens LE, Schable B, et al. Risk factors for epidemic *Xanthomonas maltophilia* infection/colonization in intensive care unit patients. *Infect Control Hosp Epidemiol*. 1992;13:201-206.
89. Wishart MM, Riley TV. Infection with *Pseudomonas maltophilia* hospital outbreak due to contaminated disinfectant. *Med J Aust*. 1976;2:710-712.
90. Simor AE, Ramage L, Wilcox L, Bull SB, Bialkowska-Hobrzanska H. Molecular and epidemiologic study of multiresistant *Serratia marcescens* infections in a spinal cord injury rehabilitation unit. *Infect Control*. 1988;9:20-27.
91. Conly JM, Klass L, Larson L, Kennedy J, Low DE, Harding GK. *Pseudomonas*

- cepacia* colonization and infection in intensive care units. *CMAJ*. 1986;134:363-366.
92. Rapkin RH. *Pseudomonas cepacia* in an intensive care nursery. *Pediatrics*. 1976; 57:239-243.
  93. Phillips I, Eykyn S, Laker M. Outbreak of hospital infection caused by contaminated autoclaved fluids. *Lancet*. 1972;1:1258-1260.
  94. Faoagali JL, Johnson RA, Smith L. Infection in a neonatal unit [letter]. *NZ Med J*. 1977;86:495.
  95. Mitchell RG, Hayward AC. Postoperative urinary-tract infections caused by contaminated irrigating fluid. *Lancet*. 1966;1:793-795.
  96. Tankovic J, Legrand P, De Gatines G, Chemineau V, Brun-Buisson C, Duval J. Characterization of a hospital outbreak of imipenem-resistant *Acinetobacter baumannii* by phenotypic and genotypic typing methods. *J Clin Microbiol*. 1994; 32:2677-2681.
  97. Beck-Sague CM, Jarvis WR, Brook JH, et al. Epidemic bacteremia due to *Acinetobacter baumannii* in five intensive care units. *Am J Epidemiol*. 1990;132: 723-733.
  98. Abrutyn E, Goodhart GL, Roos K, Anderson R, Buxton A. *Acinetobacter calcoaceticus* outbreak associated with peritoneal dialysis. *Am J Epidemiol*. 1978; 107:328-335.
  99. Wang SA, Levine RB, Carson LA, et al. Gram-negative bacteremia in a hemodialysis unit traced to portable drain port contamination. In: Program and abstracts of the 37th Interscience Conference on Antimicrobial Agents and Chemotherapy, September 28–October 1, 1997; Toronto, Ontario. Abstract J-27.
  100. Jackson BM, Beck-Sague CM, Bland LA, Arduino MJ, Meyer L, Jarvis WR. Outbreak of pyrogenic reactions and gram-negative bacteremia in a hemodialysis center. *Am J Nephrol*. 1994;14:85-89.
  101. Wang CC, Chu ML, Ho LJ, Hwang RC. Analysis of plasmid pattern in pediatric intensive care unit outbreaks of nosocomial infection due to *Enterobacter cloacae*. *J Hosp Infect*. 1991;19:33-40.
  102. Stamm WE, Colella JJ, Anderson RL, Dixon RE. Indwelling arterial catheters as a source of nosocomial bacteremia: an outbreak caused by *Flavobacterium species*. *N Engl J Med*. 1975;292:1099-1102.
  103. Boukadida J, Monastiri K, Snoussi N, Jeddi M, Berche P. Nosocomial neonatal meningitis by *Alcaligenes xylosoxidans* transmitted by aqueous eosin. *Pediatr Infect Dis*. 1993;12:696-697.
  104. Last PM, Harbison PA, Marsh JA. Bacteraemia after urological instrumentation. *Lancet*. 1966;1:74-76.
  105. Maraki S, Samonis G, Marnelakis E, Tselentis Y. Surgical wound infection caused by *Rahnella aquatilis*. *J Clin Microbiol*. 1994;32:2706-2708.
  106. Hoppe JE, Herter M, Aleksic S, Klingebiel T, Niethammer D. Catheter-related *Rahnella aquatilis* bacteremia in a pediatric bone marrow transplant recipient. *J Clin Microbiol*. 1993;31:1911-1912.
  107. Alballaa SR, Qadri SM, al-Furayh O, al-Qatary K. Urinary tract infection due to *Rahnella aquatilis* in a renal transplant patient. *J Clin Microbiol*. 1992;30:2948-2950.
  108. Pien FD, Bruce AE. Nosocomial *Ewingella americana* bacteremia in an intensive care unit. *Arch Intern Med*. 1986;146:111-112.
  109. Sirinavin S, Hotrakitya S, Suprasongsin C, Wannaying B, Pakeecheep S, Vorrachit M. An outbreak of *Salmonella urbana* infection in neonatal nurseries. *J Hosp Infect*. 1991;18:231-238.
  110. Claesson BE, Claesson UL. An outbreak of endometritis in a maternity ward caused by spread of group A streptococci from a showerhead. *J Hosp Infect*. 1985;6: 304-311.
  111. Noble MA, Isaac-Renton JL, Bryce EA, et al. The toilet as a transmission vector of vancomycin-resistant enterococci. *J Hosp Infect*. 1998;40:237-241.
  112. Dandalides PC, Rutala WA, Sarubbi FA Jr. Postoperative infections following cardiac surgery: association with an environmental reservoir in cardiothoracic intensive care unit. *Infect Control*. 1984;5:378-384.
  113. Vlodavets VV, Belokrysenko SS. The epidemiology of interhospital outbreaks of nosocomial infections. *Zh Mikrobiol Epidemiol Immunobiol*. 1984;7:75-77.
  114. Newsom SWB. Hospital infection from contaminated ice. *Lancet*. 1968;2:620-623.
  115. Bolan G, Reingold AL, Carson LA, et al. Infections with *Mycobacterium chelonae* in patients receiving dialysis and using processed hemodialyzers. *J Infect Dis*. 1985;152:1013-1019.
  116. Loudon KW, Coke AP, Burnie JP, Shaw AJ, Oppenheim BA, Morris CQ. Kitchens as a source of *Aspergillus niger* infection. *J Hosp Infect*. 1996;32:191-198.
  117. Yuen KY, Seto WH, Ching TY, Cheung WC, Kwok Y, Chu YB. An outbreak of *Candida tropicalis* in patients on intermittent peritoneal dialysis. *J Hosp Infect*. 1992;22:65-72.
  118. Fridkin SK, Kremer FB, Bland FA, Padhye A, McNeil MM, Jarvis WR. *Acremonium kiliense* endophthalmitis that occurred after cataract extraction in an ambulatory surgical center and was traced to an environmental reservoir. *Clin Infect Dis*. 1996;22:222-227.
  119. Ravn P, Lundgren JD, Kjaeldgaard P, et al. Nosocomial outbreak of cryptosporidiosis in AIDS patients. *BMJ*. 1991;302:277-280.
  120. Vincent J, Bihari DJ, Suter PM, et al. The prevalence of nosocomial infection in intensive care units in Europe: results of the European Prevalence of Infection in Intensive Care (EPIC) study. *JAMA*. 1995;274:639-644.
  121. Richards MJ, Edwards JR, Culver DH, Gaynes RP. Nosocomial infections in medical intensive care units in the United States. *Crit Care Med*. 1999;27:887-892.
  122. Petignat C, Blanc DS, Francoli P. Occult nosocomial infections. *Infect Control Hosp Epidemiol*. 1998;19:593-596.
  123. Kool JL, Fiore AE, Kioski CM, et al. More than 10 years of unrecognized nosocomial transmission of legionnaires' disease among transplant patients. *Infect Control Hosp Epidemiol*. 1998;19:898-904.
  124. Lepine AL, Jernigan DB, Butler JC, et al. A recurrent outbreak of nosocomial legionnaires' disease detected by urinary antigen testing: evidence for long-term colonization of a hospital plumbing system. *Infect Control Hosp Epidemiol*. 1998;19:905-910.
  125. Prodingier WM, Bonatti H, Allerberger F, et al. *Legionella pneumonia* in transplant recipients: a cluster of cases of eight years' duration. *J Hosp Infect Control*. 1994;26:191-202.
  126. Ciesielski C, Blaser M, Wang W. Role of stagnation and obstruction of water flow in isolation of *Legionella pneumophila* from hospital plumbing. *Appl Environ Microbiol*. 1984;48:984-987.
  127. Breiman RF, Fields BS, Sanden GN, Volmer L, Meier A, Spika JS. Association of shower use with Legionnaire's disease: possible role of amoebae. *JAMA*. 1990; 263:2924-2926.
  128. Yu VL. Could aspiration be the major mode of transmission for *Legionella*? *Am J Med*. 1993;95:13-15.
  129. Marrie T, Haldane D, MacDonald S. Control of endemic nosocomial Legionnaire's disease by using sterile potable water for high risk patients. *Epidemiol Infect*. 1991;107:591-605.
  130. Ruchel R, Wilichowski E. Cerebral *Pseudallescheria mycosis* after near drowning. *Mycoses*. 1995;38:473-475.
  131. Perz JF, Ennever FK, Le Blancq SM. *Cryptosporidium* in tap water: comparison of predicted risks with observed levels of disease. *Am J Epidemiol*. 1998;147: 289-301.
  132. Hoxie MJ, Davis JP, Vergeront JM, Nashold RD, Blair KA. Cryptosporidiosis-associated mortality following a massive waterborne outbreak in Milwaukee, Wisconsin. *Am J Public Health*. 1997;87:2032-2035.
  133. Department of the Environment and Department of Health. *Cryptosporidium in Water Supplies: Second Report of the Group of Experts (Badenoch Report)*. London, England: HMSO; 1995.
  134. US Environmental Protection Agency and Centers for Disease Control and Prevention. *Guidance for People With Severely Weakened Immune Systems*. 1999. Document No. EPA 816-F-99-005. Available at: <http://www.epa.gov/safewater/crypto.html>. Accessed September 2001.
  135. US Environmental Protection Agency. *Water on Tap: A Consumer's Guide to the Nation's Drinking Water*. 1997. Document No. EPA 815-K-97-002. Available at: <http://www.epa.gov/OGWDW/wot/ontap.html>. Accessed September 2001.
  136. Tablan O. Nosocomial pneumonia. In: Olmsted RN, ed. *APIC Infection Control and Applied Epidemiology: Principles and Practice*. St Louis, Mo: Mosby-Year Book Inc; 1996:10.1-10.14.
  137. CDC, Infectious Disease Society of America, and American Society of Blood and Marrow Transplantation. Guidelines for preventing opportunistic infections among hematopoietic stem cell transplant recipients. *MMWR Morb Mortal Wkly Rep*. 2000;49:1-128.
  138. Addiss D, Pond RS, Remshak M, Juranek DD, Stokes S, Davis JP. Reduction of risk of watery diarrhea with point-of-use water filters during a massive outbreak of waterborne *Cryptosporidium* infection in Milwaukee, Wisconsin, 1993. *Am J Trop Med Hyg*. 1996;54:549-553.
  139. Skewes SM. No more bed baths. *RN*. 1994;57:34-35.
  140. Bartley J. Water. In: Olmsted RN, ed. *APIC Infection Control and Applied Epidemiology: Principles and Practice*. St Louis, Mo: Mosby-Year Book Inc; 1996: 118.1-118.4.
  141. Jenner EA, Mackintosh C, Scott GM. Infection control: evidence into practice. *J Hosp Infect*. 1999;42:91-104.
  142. Goetz A YV. *Legionella* species. In: Olmsted RN, ed. *APIC Infection Control and Applied Epidemiology: Principles and Practice*. St Louis, Mo: Mosby-Year Book Inc; 1996:64.1-64.4.
  143. Yu VL. Resolving the controversy on environmental cultures for *Legionella*: a modest proposal. *Infect Control Hosp Epidemiol*. 1998;19:893-897.
  144. Cooke RPD, Whymant-Morris A, Umasankar RS, Goddard SV. Bacteria-free water for automatic washer-disinfectors: an impossible dream? *J Hosp Infect*. 1998; 39:63-65.
  145. Geldreich EE. Characterizing the distribution system: microbial issues. In: Geldreich EE, ed. *Microbial Qualities of Water Supply in Distribution Systems*. Boca Raton, Fla: CRC Press Inc; 1996:1-37.