Legionella in Domestic Water Systems

Subjects: Biotechnology & Applied Microbiology

Contributor: Maria Anna Coniglio

Legionella is able to remain in water as free-living planktonic bacteria or to grow within biofilms that adhere to the pipes. It is also able to enter amoebas or to switch into a viable but not culturable (VBNC) state, which contributes to its resistance to harsh conditions and hinders its detection in water.

Keywords: Legionella ; water systems ; Water Safety Plan

1. Introduction

Legionella colonization of building potable water systems implies many Public Health concerns, especially for more fragile persons (elderly adults, smokers or people with weakened immune systems), which are particularly susceptible to the infection and at risk for developing clinical complications and respiratory failure. Obviously, as the population ages, the health impact on 'at risk' groups of legionellosis is likely to continue to increase.

2. Disinfection Strategies

2.1. Oxidizing Agents

Chlorine is widely used for its strong oxidizing power for primary disinfection treatment of potable water. It reacts with a variety of bacterial cellular components $^{[\underline{1}]}$ and is able to permeabilize the cytoplasmic membranes causing leakage of proteins and DNA damage $^{[\underline{2}]}$. In order to inactivate microbial contaminants or to prevent a possible microbial regrowth in water distribution systems, the World Health Organization (WHO) recommends 0.5 mgL⁻¹ for free chlorine $^{[\underline{3}]}$.

L. pneumophila has shown resistance to high levels of chlorine by the formation of biofilms $^{[\underline{4}]}$, and pipes corrosion can be expected when the disinfectant is dosed in a water distribution system. In particular, high levels of residual chlorine are responsible for copper and iron pipes corrosion, while lead may not experience increased corrosion $^{[\underline{5}][\underline{6}]}$. Maintaining the pH of the chlorinated water above 8 may counteract the corrosive effect of chlorine on copper and iron. Blends of polyand orthophosphates can be used as corrosion inhibitors in order to create a passivating film on the pipe wall. However, the use of polyphosphates for corrosion control entails considerable uncertainty and risk because they may increase the leaching of pipe metal into the water $^{[\underline{7}]}$.

Finally, the formation of potentially toxic and carcinogenic disinfection by-products (DBPs) has been identified in chlorinated drinking waters. The trihalomethanes (THMs) are likely to be the main chlorine DBPs. Because they usually occur together, total THMs are considered as a group, with an allowable concentration in drinking water ranging from 80 $\mu g L^{-1}$ [9] to 100 $\mu g L^{-1}$ [9]. THMs are formed by the interaction of aqueous-free chlorine with soluble, natural organic compounds present in water and their concentrations tend to increase with the presence of bromide or iodide, as well as with the increase of temperature, pH, and chlorine dosage [10]. Removal of THMs or their precursors is difficult and involves resource-intensive processes [11] like for example ozonation and biological granular activated carbon [12] or magnetic graphene oxide [13]. Nevertheless, the technologies described above could be time-consuming and extremely expensive. For this reason, an effective method to control DBPs in drinking water may be the use of alternative disinfectants.

Chlorine dioxide is a water-soluble gas that can easily diffuse through bacterial cell membranes. When compared to chlorine, chlorine dioxide has been found to be superior in penetrating biofilms $^{[14]}$ and in inactivating free-living protozoa such as Acanthamoeba strains $^{[15]}$.

It has been demonstrated that using chlorine dioxide as secondary disinfectant can significantly reduce the risk of acquiring Legionnaires' disease in hospital settings $\frac{[16][17][18]}{[18]}$. A total chlorine dioxide residual of 0.1–0.5 mgL⁻¹ at the tap

is usually sufficient to control *Legionella* colonization, but higher residuals may be necessary in heavily colonized water systems $^{[19]}$.

Chlorine dioxide is less corrosive than chlorine [14]. Nevertheless, there is evidence that it can cause damage to polyethylene pipes [20][21]. Finally, although it does not form appreciable amounts of THMs and halo acetic acids (HAAs), it has been seen that on-site generation of chlorine dioxide often involves the production of free chlorine, which tend to increase with reaction time. Therefore, the ratio of chlorine dioxide to chlorine needs to be constantly monitored and possibly adjusted to obtain the best control of DBPs formation [22].

Monochloramine is formed by the reaction of ammonia with chlorine. For primary disinfection of drinking water, the target concentration for the disinfectant is $1.5-3.0~\text{mgL}^{-1}$ as Cl2 but the optimal concentrations may depend on the manufacturer. The WHO recommends $3~\text{mgL}^{-1}$ [23] while the Environmental Protection Agency (EPA) concentration is $4.0~\text{mgL}^{-1}$ as Cl2 [24]. However, monochloramine is often used as a secondary disinfectant after primary treatment with chlorine, especially in distribution systems heavily colonized by Legionella [25].

Monochloramine seems to react slowly with nucleic acids but rapidly with several amino acids, with little damage to bacterial membranes ^[26]. This could explain why measurements of free chlorine and monochloramine biofilm penetration show that monochloramine is more effective at penetrating biofilms than is free chlorine, although increased penetration does not correlate with greater inactivation of biofilm microorganisms. However, monochloramine has shown to be more effective on copper biofilms while free chlorine is more effective on polyvinyl chloride drinking water biofilms ^[27]. Finally, the lower reactivity of monochloramine can also be an advantage, as it is less likely to react with natural organic matter in the water, forming fewer DBPs, and leading to fewer undesirable tastes and odors than chlorine or chlorine dioxide ^[28].

The main disadvantage of monochlorination of the water is the nitrification by nitrifying bacteria of ammonia or free ammonia released by the decay of the disinfectant. Nitrification results in the formation of toxic nitrite in the distribution system. Moreover, the nitrification process has the potential to locally lower the pH in alkaline waters and cause corrosion of elastomeric materials. Factors influencing nitrification include the rate at which monochloramine residual decays, microbial regrowth, corrosion of pipe materials, as well as biofilm formation. Biofilm, in particular, facilitates the growth of nitrifying bacteria, promoting nitrification in water systems $\frac{[29][30]}{2}$. One way to potentially control nitrification in premise plumbing systems is through the development of specific building management plans. Optimizing the chlorine-to-ammonia ratio, typically 5:1 $\frac{[31]}{2}$, flushing out the outlets $\frac{[32]}{2}$, decreasing monochloramine residence time in service reservoirs $\frac{[33]}{2}$, chlorite addition $\frac{[34]}{2}$, reducing natural organic matter and preventing biofilm formation $\frac{[35][36][37]}{2}$, as well as controlling the pH $\frac{[38][39]}{2}$ may be effective methods of controlling and preventing nitrite formation.

Ozone is considered the most efficient disinfectant for all types of microorganisms because it is able to oxidize the cell membrane and wall constituents of a bacterial cell, as well as enzymes and nucleic acids. Under experimental conditions, it has demonstrated to be more effective at inactivating \underline{L} . $\underline{pneumophila}$ than other disinfectants $\underline{[40][41]}$. Nonetheless, determination of the in vitro activity of ozone against the bacterium does not predict the efficacy of its eradication from water fixtures $\underline{[42]}$. In fact, studies in real water systems show no significant reduction in $\underline{Legionella}$ colonization $\underline{[43][44]}$.

Its low effectiveness against *Legionella* is probably due to the fact that ozone does not stay in water sufficiently long to provide a residual effect. For this reason, chlorine can be added after ozonation, but DBPs may be produced by their combinations. In fact, the vast majority of the ozone DBPs identified up to now contain oxygen in their structures, with no halogenated DBPs observed except when chlorine or chloramines are applied as a secondary disinfectant $^{[45]}$. Moreover, there is evidence that the use of ozone as a primary disinfectant may cause a shift to more brominated DBPs during subsequent chlorination $^{[46]}$.

Hydrogen peroxide is a strong oxidizing agent that oxidizes microorganisms' enzymatic systems, releasing free oxygen atoms without the formation of DBPs. The European directive established a concentration limit for hydrogen peroxide in drinking water of 25 mgL⁻¹ [47]. While the US Environmental Protection Agency $^{[48]}$ guidelines recommend 25–50 ppm of residual hydrogen peroxide in drinking water. Concentrations of 25 mgL⁻¹ have demonstrated good efficacy in controlling Legionella colonization of water networks, with a higher disinfection power with the increase of the water temperature up to 40–50 °C $^{[49][50]}$. Finally, to enhance its activity, hydrogen peroxide is sometimes used in combination with other oxidants such as ozone, silver, or UV irradiation.

2.2. Non-Oxidizing Agents

Copper–silver ionization is commonly used in water distribution systems with hot water recirculating loops $\frac{[14]}{}$. When used together, copper and silver ions create a synergistic effect. In fact, the copper ions destroy the cell wall permeability, which

allows the silver ions to interfere with the synthesis of proteins and enzymes, thus resulting in a higher inactivation rate of *L. pneumophila* $\frac{[51]}{}$. For Legionella control, the recommended copper and silver ion concentrations are 0.2–0.4 mgL⁻¹ and 0.02–0.04 mgL⁻¹, respectively $\frac{[14]}{}$.

Literature data show that there are at least three major challenges facing copper–silver ionization [52][53][54]: (i) ensuring that the added ions are flushed throughout the entire water distribution system, (ii) the emergence of resistant legionellae, and (iii) the reduction in the microbiocidal power due to the formation of metal complexes. Finally, copper–silver ionization may increase chlorine DBPs formation at pH 8.6 in the presence of natural organic matter [55].

Short-wavelength UV is believed to have biocidal effects through a molecular rearrangement of the purine and pyrimidine components of the nucleoproteins, which hampers DNA replication ^[56]. Breaks in the bonding structure also occur ^[57]. Nevertheless, the current technology of low-pressure (LP) mercury lamps that is used for UV irradiation has several shortcomings.

First of all, *Legionella* is able to repair damages to DNA [58]. Secondly, the maximum absorbance of nucleic acids is around 260 nm, while proteins have a relative maximum absorbance of around 280 nm [59]. Thus, targeting one of the components of the bacterial cell may be more effective in *Legionella* inactivation [60]. LP mercury lamps emit at 254 nm, and this may result in a low efficacy of inactivation. On the contrary, the irradiation technology using light emitting diodes (LEDs) can emit at many different wavelengths in the UV-B and UV-C. Moreover, LP lamps contain mercury, which is toxic to the environment, while LEDs are made of gallium/aluminum nitride or aluminum nitride, which are not toxic nor hazardous.

Regardless its technology, UV light produces no residual. Therefore, if a residual is desired, another disinfectant must be used. To this regard, the application of UV light to shower heads and faucets in hospitals has indicated that the technology alone is insufficient to control *Legionella*, and other disinfection measures have to be used along with UV irradiation for an effective control of the colonization [56]. Finally, UV light shows poor penetration in biofilms [61].

2.3. Point-of-Use (POU) Filtration

Disinfectants may not reach dead legs or low water flow areas. Furthermore, they can dissipate through the plumbing system, making them less effective at distal points, and secondary chemical water disinfection may shorten the life of the pipes. For these reasons, point-of-use (POU) filtration can be regarded as an additional barrier to add to other primary treatment technologies to prevent exposure to legionellae, particularly in hospital settings. The filters are attached to individual faucets and showers, providing a physical barrier between Legionella and high-risk patients. Anyway, a recommendation for their use cannot be made until an evaluation of their efficacy has been performed [62].

It has been seen, for example, that the application of carbon filters may result in a greater presence of *Legionella* in water because the bacterium can colonize the filters while passing through $\frac{[63][64]}{}$. On the contrary, membrane filters have shown to control the colonization of hospital water systems up to 2–8 weeks of continuous use $\frac{[65][66]}{}$, especially when they are covered with a silver layer $\frac{[67]}{}$. More recently, the novel electrically heatable carbon nanotube (CNT) point-of-use (POU) filters have demonstrated to remove 99.9% of *L. pneumophila* in water $\frac{[68]}{}$.

Obviously, one filter is needed for each fixture, and if the filters are not regularly replaced, Legionella can colonize them regardless of their technology. Therefore, replacing these filters may be expensive. For this reason, the use of filters, which requires fewer change-outs, could be a cost-effective method for preventing hospital-acquired Legionnaires' disease $\frac{[69]}{[69]}$.

References

- 1. Shang, C.; Blatchley, E.R. Differentiation and quantification of free chlorine and inorganic chloramines in aqueous soluti on by MIMS. Environ. Sci. Technol. 1999, 33, 2218–2223.
- 2. Virto, R.; Mañas, P.; Álvarez, I.; Condon, S.; Raso, J. Membrane damage and microbial inactivation by chlorine in the a bsence and presence of a chlorine-demanding substrate. Appl. Environ. Microbiol. 2005, 71, 5022–5028.
- 3. World Health Organization. Chlorine in Drinking-Water; World Health Organization: Geneva, Switzerland, 2003; p. 11. A vailable online: (accessed on 10 February 2021).
- 4. Cooper, I.R.; White, J.; Mahenthiralingam, E.; Hanlon, G.W. Long-term persistence of a single Legionella pneumophila strain possessing the mip gene in a municipal shower de-spite repeated cycles of chlorination. J. Hosp. Infect. 2008, 7

- 5. García-Ávila, F.; Del Pino, L.F.; Bonifaz, G.A.; Zhindòn-Arévalo, C.; Ramos-Fernàndez, L.; Garcìa-Altamirano, D.; Sanc hez, C. Effect of chlorine residual on copper pipes in drinking water systems. J. Eng. Sci. Technol. Rev. 2019, 12, 119–126
- 6. Cantor, A.F.; Park, J.K.; Vaiyavatjamai, P. The effect of chlorine on corrosion in drinking water systems. J. Am. Water W ork. Assoc. AWWA 2003, 95, 112–123.
- 7. Holm, T.R.; Schock, M.R. Potential effects of polyphosphate products on lead solubility in plumbing systems. J. Am. Wa ter Work. Assoc. AWWA 1991, 83, 76.
- 8. US EPA. EPA Drinking Water Guidance on Disinfection By-Products Advice Note No. 4. Version 2. Disinfection By-Products in Drinking Water. 2001. Available online: (accessed on 10 February 2021).
- 9. Council Directive 98/83/EC of 3 November 1998 on the Quality of Water Intended for Human Consumption. 1998. Avail able online: (accessed on 10 February 2021).
- 10. Nikolau, A.D.; Golfinopoulos, S.K.; Arhonditsis, G.B.; Kolo-voyiannis, V.; Lekkas, T.D. Modeling the formation of chlorina tion by-products in river waters with different quality. Chemosphere 2004, 55, 409–420.
- 11. Teksoy, A.; Alkan, U.; Başkaya, H.S. Influence of the treatment process combinations on the formation of THM species i n water. Sep. Purif. Technol. 2008, 61, 447–454.
- 12. Yan, M.; Wang, D.; Ma, X.; Ni, J.; Zhang, H. THMs precursor removal by an integrated process of ozonation and biological granular activated carbon for typical Northern China water. Sep. Purif. Technol. 2010, 72, 263–268.
- 13. Liu, Z.; Wang, X.; Luo, Z.; Huo, M.; Wu, J.; Huo, H.; Yang, W. Removing of disinfection-by-products precursors from sur face water by using magnetic graphene oxide. PLoS ONE 2015, 10, e0143819.
- 14. Lin, Y.E.; Stout, J.E.; Yu, V.L. Controlling Legionella in hospital drinking water: An evidence-based review of disinfection methods. Infect. Control Hosp. Epidemiol. 2011, 32, 166–173.
- 15. Dupuy, M.; Mazoua, S.; Berne, F.; Bodet, C.; Garrec, N.; Herbelin, P.; Menard-Szczebara, F.; Oberti, S.; Rodier, M.H.; S oreau, S.; et al. Efficiency of water disinfectants against Legionella pneumophila and Acanthamoeba. Water Res. 2011, 45, 1087–1094.
- 16. Zhang, Z.; Mccann, C.; Hanrahan, J.; Jencson, A.; Joyce, D.; Fyffe, S.; Piesczynski, S.; Hawks, R.; Stout, J.E. Legionell a control by chlorine dioxide in hospital water systems. J. Am. Water Work. Assoc. AWWA 2009, 101, 117–127.
- 17. Marchesi, I.; Marchegiano, P.; Bargellini, A.; Cencetti, S.; Frezza, G.; Miselli, M.; Borella, P. Effectiveness of different m ethods to control legionella in the water supply: Ten-year experience in an Italian university hospital. J. Hosp. Infect. 20 11, 77, 47–51.
- 18. Casini, B.; Buzzigoli, A.; Cristina, M.L.; Spagnolo, A.M.; DelGiudice, P.; Brusaferro, S.; Poscia, A.; Moscato, U.; Valentin i, P.; Baggiani, A.; et al. Long-term effects of hospital water network disinfection on Legionella and other waterborne ba cteria in an Italian University Hospital. Infect. Control Hosp. Epidemiol. 2014, 35, 293–299.
- 19. Health and Safe Executive (HSE). Legionnaires' Disease. Part 2: The Control of Legionella Bacteria in Hot and Cold W ater Systems. 2014. Available online: (accessed on 9 February 2021).
- 20. Chord, F.; Fascia, P.; Mallaval, F.; Cornillon, J.; Roesch, L.; Pozzetto, B.; Grattard, F.; Berthelot, P. Chlorine dioxide for Legionella spp. disinfection: A danger for cross-linked polyethylene pipes? J. Hosp. Infect. 2011, 78, 242–243.
- 21. Yu, W.; Azhdar, B.; Anderson, D.; Reitberger, T.; Hassinen, J.; Hjertberg, T.; Gedde, U.W. Deterioration of polyethylene pipes exposed to water containing chlorine dioxide. Polym. Degrad. Stabil. 2011, 96, 790–797.
- 22. Gan, W.; Huang, H.; Yang, X.; Peng, Z.; Chen, G. Emerging investigators series: Disinfection-by-products in mixed chlorine dioxide and chlorine water treatment. Environ. Sci. Water Res. Technol. 2016, 2, 838.
- 23. World Health Organization. Monochloramine in Drinking-Water. 2004. Available online: (accessed on 10 February 202 1).
- 24. Alexander, M.T.; Waters, T.E.; Smith, G.A.; Wahman, D.G. New EPA Method to Determine Monochloramine Concentrati on in Drinking Water. In Proceedings of the 17th Annual EPA Drinking Water Workshop: Small System Challenges and Solutions, Covington, KY, USA, 1–3 September 2020.
- 25. Coniglio, M.A.; Ferrante, M.; Yassin, M.H. Preventing Healthcare-Associated Legionellosis: Results after 3 Years of Continuous Disinfection of Hot Water with Monochloramine and an Effective Water Safety Plan. Int. J. Environ. Res. Public Health 2018, 15, 1594.
- 26. Jacangelo, J.G.; Olivieri, V.P.; Kawata, K. Investigating the mechanism of inactivation of Escherichia coli B by monochlo ramine. J. Am. Water Work. Assoc. 1991, 83, 80–87.

- 27. Buse, H.Y.; Morris, B.J.; Struewing, I.T.; Szaboa, J.G. Chlorine and Monochloramine Disinfection of Legionella pneumo phila Colonizing Copper and Polyvinyl Chloride Drinking Water Biofilms. Appl. Environ. Microbiol. 2019, 85, 02956–030 18.
- 28. Marchesi, I.; Paduano, S.; Frezza, G.; Sircana, L.; Vecchi, E.; Zuccarello, P.; Conti, G.; Ferrante, M.; Borella, P.; Bargell ini, A. Safety and Effectiveness of Monochloramine Treatment for Disinfecting Hospital Water Networks. Int. J. Environ. Res. Public Health 2020, 17, 6116.
- 29. Schramm, A.; Beer, D.; Gieseke, A.; Amann, R. Microenvironments and distribution of nitrifying bacteria in a membrane -bound biofilm. Environ. Microbiol. 2000, 2, 680–686.
- 30. Lipponen, M.; Martikainen, P.; Vasara, R.; Servomaa, K.; Zacheus, O.; Kontro, M. Occurrence of nitrifiers and diversity of ammonia-oxidizing bacteria in developing drinking water biofilms. Water Res. 2004, 38, 4424–4434.
- 31. Lieu, N.; Wolfe, R.; Means, E., III. Optimizing Chloramine Disinfection for the Control of Nitrification. J. Am. Water Work. Assoc. 1993, 85, 84–90.
- 32. Nguyen, C.; Elfland, C.; Edwards, M. Impact of advanced water conservation features and new copper pipe on rapid ch loramine decay and microbial regrowth. Water Res. 2012, 46, 611–621.
- 33. Senevirathna, L.; Sathasivan, A.; Kastl, G. Forecasting the chloramine residual in service reservoirs from online measur ement. Desalin. Water Treat. 2015, 57, 7943–7950.
- 34. McGuire, M.J.; Wu, X.; Blute, N.K.; Askenaizer, D.; Qin, G. Prevention of nitrification using chlorite iron: Results of a de monstration project in Glendale, Calif. J. Am. Water Work. Assoc. AWWA 2009, 101, 47–59.
- 35. Williams, K.; Pruden, A.; Falkinham, J.O.; Edwards, M. Relationship between Organic Carbon and Opportunistic Pathogens in Simulated Glass Water Heaters. Pathogens 2015, 4, 355–372.
- 36. Vikesland, P.; Ozekin, K.; Valentine, R. Effect of Natural Organic Matter on Monochloramine decomposition: Pathway El ucidation through the Use of Mass and Redox Balances. Environ. Sci. Technol. 1998, 32, 1409–1416.
- 37. Proctor, C.R.; Dai, D.; Edwards, M.A.; Pruden, A. Interactive effects of temperature, organic carbon, and pipe material on microbiota composition and Legionella pneumophila in hot water plumbing systems. Microbiome 2017, 5, 130.
- 38. Loveless, J.; Painter, H. The Influence of Metal Ion Concentrations and pH Value on the Growth of a Nitrosomonas Stra in Isolated from Activated Sludge. Microbiology 1968, 52, 1–14.
- 39. Wilczak, A. Chloramine Decay Rate: Factors and Research Needs. In Proceedings of the 2001 AWWA Annual Confere nce Proceedings, Washington, DC, USA, 17–21 June 2001.
- 40. Domingue, E.L.; Tyndall, R.L.; Mayberry, W.R.; Pancorbo, O.C. Effects of three oxidizing biocides on Legionella pneum ophila serogroup 1. Appl. Environ. Microbiol. 1988, 54, 741–747.
- 41. McGrane, W.K. Ozone, a study of the effects of biocides on Legionella pneumophila. Ind. Water Treat. 1995, 27, 28–3 2.
- 42. Edelstein, P.H.; Whittaker, R.E.; Kreiling, R.L.; Howell, C.L. Efficacy of ozone in eradication of Legionella pneumophila f rom hospital plumbing fixtures. Appl. Environ. Microbiol. 1982, 44, 1330–1333.
- 43. Blanc, D.S.; Carrara, P.; Zanetti, G.; Francioli, P. Water disinfection with ozone, copper and silver ions, and temperature increase to control Legionella: Seven years of experience in a university teaching hospital. J. Hosp. Infect. 2005, 60, 69 –72.
- 44. Nogueira, R.; Utecht, K.U.; Exner, M.; Verstraete, W.; Rosenwinkel, K.H. Strategies for the reduction of Legionella in bi ological treatment systems. Water Sci. Technol. 2016, 4, 816–823.
- 45. Richardson, S.D.; Thruston, A.D., Jr.; Caughran, T.V.; Chen, P.H.; Collette, T.W.; Floyd, T.L.; Schenck, K.M.; Lykins, B. W., Jr.; Sun, G.R.; Majetich, G. Identification of new ozone disinfection by products in drinking water. Environ. Sci. Tech nol. 1999, 33, 3368–3377.
- 46. Mao, Y.; Wang, X.; Yang, H.; Wang, H.; Xie, Y.F. Effects of ozonation on disinfection byproduct formation and speciation during subsequent chlorination. Chemosphere 2014, 117, 515–520.
- 47. Regulation (EU) No 528/2012 Concerning the Making Available on the Market and Use of Biocidal Products Evaluation of Active Substances Assessment. Report Hydrogen Peroxide. 2015. Available online: (accessed on 12 February 202 1).
- 48. USEPA. Alternative Disinfectants and Oxidants Guidance Manual. Office of Water 815-R-99-014. 1999. Available onlin e: (accessed on 12 February 2021).
- 49. Ditommaso, S.; Giacomuzzi, M.; Ricciardi, E.; Zotti, C.M. Efficacy of a Low Dose of Hydrogen Peroxide (Peroxy Ag+) fo r Continuous Treatment of Dental Unit Water Lines: Challenge Test with Legionella pneumophila Serogroup 1 in a Simu lated Dental Unit Waterline. Int. J. Environ. Res. Public Health 2016, 13, 745.

- 50. Casini, B.; Aquino, F.; Totaro, M.; Miccoli, M.; Galli, I.; Manfredini, L.; Giustarini, C.; Costa, A.L.; Tuvo, B.; Valentini, P.; e t al. Application of Hydrogen Peroxide as an Innovative Method of Treatment for Legionella Control in a Hospital Water Network. Pathogens 2017, 6, 15.
- 51. Landeen, L.K.; Moyasar, Y.; Gerba, C. Efficacy of copper and silver ions and reduced levels of free chlorine in inactivati on of Legionella pneumophila. Appl. Environ. Microbiol. 1989, 55, 3045–3050.
- 52. Rohr, U.; Senger, M.; Selenka, F.; Turley, R.; Wilhelm, M. Four years of experience with silver-copper ionization for cont rol of Legionella in German University Hospital hot water plumbing system. Clin. Infect. Dis. 1999, 29, 1507–1511.
- 53. Lin, Y.S.; Vidic, R.D.; Stout, J.E.; Yu, V.L. Negative effect of high pH on biocidal efficacy of copper and silver ions in con trolling Legionella pneumophila. Appl. Environ. Microbiol. 2002, 68, 2711–2715.
- 54. Pérez-Cachafeiro, S.; Mato, I.; Gonzàles Garcìa, I. Is copper-silver ionization safe and effective in controlling Legionell a? J. Hosp. Infect. 2007, 67, 209–216.
- 55. Zhang, H.; Andrews, S.A. Catalysis of copper corrosion products on chlorine decay and HAA formation in simulated dist ribution systems. Water Res. 2012, 46, 2665–2673.
- 56. Liu, Z.; Stout, J.E.; Tedesco, L.; Boldin, M.; Hwang, C.; Yu, V.L. Efficacy of ultraviolet light in preventing Legionella colo nization of a hospital water distribution system. Water Res. 1995, 29, 2275–2280.
- 57. Kim, T.; Silva, J.L.; Chen, T.C. Effects of UV irradiation on selected pathogens in peptone water and on stainless steel a nd chicken meat. J. Food Prot. 2002, 65, 1142–1145.
- 58. Charpentier, X.; Kay, E.; Schneider, D.; Shuman, H.A. Antibiotics and UV radiation induce competence for natural transf ormation in Legionella pneumophila. J. Bacteriol. 2011, 193, 1114–1121.
- 59. Vilhunen, S.; Sarkka, J.; Silanpaa, M. Ultraviolet Light-Emitting Diodes in Water Disinfection. Environ. Sci. Pollut. Res. 2009, 16, 439–442.
- 60. Chevremont, A.C.; Farnet, A.M.; Coulomb, B.; Boudenne, J.L. Effect of Coupled UV-A and UV-C LEDs on Both Microbi ological and Chemical Pollution of Urban Wastewaters. Sci. Total Environ. 2012, 426, 304–310.
- 61. De Carvalho, C.C.C.R. Biofilms: Microbial Strategies for Surviving UV Exposure. In Ultraviolet Light in Human Health, Diseases and Environment. Advances in Experimental Medicine and Biology; Ahmad, S., Ed.; Springer: Cham, Switzerl and, 2017; p. 996.
- 62. Parkinson, J.; Baron, J.L.; Hall, B.; Bos, H.; Racine, P.; Wagener, M.M.; Stout, J.E. Point-of-use filters for prevention of health care—Acquired Legionnaires' disease: Field evaluation of a new filter product and literature review. Am. J. Infect. Control 2020, 48, 132–138.
- 63. Molloy, S.L.; Ives, R.; Hoyt, A.; Taylor, R.; Rose, J.B. The use of copper and silver in carbon point-of-use filters for the s uppression of Legionella throughput in domestic water systems. Appl. Microbiol. 2008, 104, 998–1007.
- 64. Wu, C.C.; Ghosh, S.; Martin, K.J.; Pinto, A.J.; Denef, V.J.; Olson, T.M.; Love, N.G. The microbial colonization of activate d carbon block point-of-use (PoU) filters with and without chlorinated phenol disinfection by-products. Environ. Sci. Wat er Res. Technol. 2017, 3, 830–843.
- 65. Sheffer, P.J.; Stout, J.E.; Wagener, M.M.; Muder, R.R. Efficacy of new point-of-use water filter for preventing exposure t o Legionella and waterborne bacteria. Am. J. Infect. Control 2005, 33, 20–25.
- 66. Baron, J.L.; Peters, T.; Shafer, R.; MacMurray, B.; Stout, J.E. Field evaluation of a new point-of-use faucet filter for preventing exposure to Legionella and other waterborne pathogens in health care facilities. Am. J. Infect. Control 2014, 42, 1193–1196.
- 67. Vonberg, R.P.; Sohr, D.; Bruderek, J.; Gastmeier, P. Impact of a silver layer on the membrane of tap water filters on the microbiological quality of filtered water. BMC Infect. Dis. 2008, 8, 133.
- 68. Oh, Y.; Noga, R.; Shanov, V.; Ryu, H.; Chandra, H.; Yadav, B.; Yadav, J.; Chae, S. Electrically heatable carbon nanotub e point-of-use filters for effective separation and in-situ inactivation of Legionella pneumophila. Chem. Eng. J. 2019, 36 6, 21–26.
- 69. Oyanedel-Craver, V.A.; Smith, J.A. Sustainable Colloidal-Silver-Impregnated Ceramic Filter for Point-of-Use Water Trea tment. Environ. Sci. Technol. 2008, 42, 927–933.