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MINIREVIEW

Quaternary Ammonium Biocides: Efficacy in Application

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Quaternary ammonium compounds (QACs) are among the most commonly used disinfectants. There has been concern that their widespread use will lead to the development of resistant organisms, and it has been suggested that limits should be place on their use. While increases in tolerance to QACs have been observed, there is no clear evidence to support the development of resistance to QACs. Since efflux pumps are believe to account for at least some of the increased tolerance found in bacteria, there has been concern that this will enhance the resistance of bacteria to certain antibiotics. QACs are membrane-active agents interacting with the cytoplasmic membrane of bacteria and lipids of viruses. The wide variety of chemical structures possible has seen an evolution in their effectiveness and expansion of applications over the last century, including non-lipid-containing viruses (i.e., noroviruses). Selection of formulations and methods of application have been shown to affect the efficacy of QACs. While numerous laboratory studies on the efficacy of QACs are available, relatively few studies have been conducted to assess their efficacy in practice. Better standardized tests for assessing and defining the differences between increases in tolerance versus resistance are needed. The ecological dynamics of microbial communities where QACs are a main line of defense against exposure to pathogens need to be better understood in terms of sublethal doses and antibiotic resistance.

Biocides (disinfectants) play a critical role in controlling the spread of environmentally transmitted pathogens in health care and food-processing environments, as well as in the home. This review looks at a class of antimicrobials called quaternary ammonium compounds (QACs), with emphasis on understanding how formulations impact efficacy against target organisms and on the significance of resistance and cross-resistance with antibiotics in actual in-use applications.

The quaternary nitrogen moiety occurs naturally in living systems, where it plays an important role in various biological processes (1). The first synthesis and recognition of their antimicrobial activity occurred almost 100 years ago (1), but it was not until after World War II that QACs came into widespread use. Today, they are used in numerous consumer products and in the food and health care industries for cleaning, sanitizing, and disinfecting surfaces. Their low toxicity and ability to be formulated for specific applications and target organisms help account for their widespread use.

QACs are cationic detergents (surfactants or surface-active agents). They reduce surface tension and form micelles, allowing dispersion in a liquid. The basic QAC structure is show in Fig. 1.

The cation portion consists of the central nitrogen with four attached groups, which occur in a variety of structures (2). The negatively charged anion portion (X^-) is usually chlorine or bromine and is linked to the nitrogen to form the QAC salt. QACs are further classified on the basis of the nature of the R groups, which can include the number of nitrogen atoms, branching of the carbon chain, and the presence of aromatic groups. These variations can affect the antimicrobial activity of the QAC in terms of dose and action against different groups of microorganisms. Examples of the structures of three common QACs are shown in Fig. 2. The length of the R groups can also greatly affect their antimicrobial activity. Methyl group lengths of C_{12} to C_{16} usually show the greatest antimicrobial activity.

Many antimicrobial products contain mixtures of QACs and other adjuncts to increase their efficacy or to target a specific group of organisms (3). The wide variety of chemical structures possible with QACs has allowed an evolution of their effectiveness and an expansion of their applications over the last century (Table 1). This has resulted in a continued increase in efficacy while reducing costs and lowering toxicity (1).

Mechanism of action. QACs are membrane-active agents interacting with the cytoplasmic membrane of bacteria and the plasma membrane of yeast. Their hydrophobic activity also makes them effective against lipid-containing viruses. QACs also interact with intracellular targets and bind to DNA (4). They are also effective against non-lipid-containing viruses and spores, depending on the product formulation (Table 2). At low concentrations (0.5 to 5 mg/liter) they are algistatic, bacteriostatic, tuberculostatic, sporostatic, and fungistatic. At concentrations of 10 to 50 mg/liter, they are microbicidal for these same groups, depending upon the specific organism and formulation (1).

McDonnell proposed the following series of events involved in the action of QACs against microorganisms: (i) QAC adsorption to and penetration of the cell wall; (ii) reaction with the cytoplasmic membrane (lipid or protein), followed by membrane disorganization; (iii) leakage of intracellular lower-weight material; (iv) degradation of proteins and nucleic acids; and (v) cell wall lysis caused by autolytic enzymes (2).

Various formulations of QACs have been shown to be active against a wide variety of microbial types, as shown in Table 2.

Assessment of QAC activity. In the United States, the Envi-

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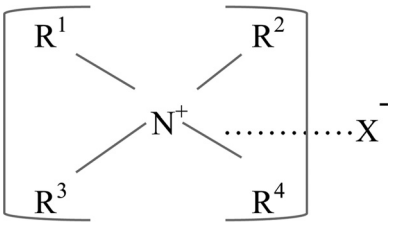

FIG 1 Basic structure of QACs.

TABLE 1 Evolution of quaternary ammonium disinfectants

Generation (yr)	Compound(s)
1st	Benzalkonium, alkyl chains, C_{12} to C_{18}
2nd	Aromatic rings with hydrogen and chlorine, methyl and ethyl groups
3rd (1955)	Dual QACs; mixture of alkyl dimethyl benzyl ammonium chloride (lower toxicity)
4th	Dialkylmethyl aminos with twin chains
5th	Synergistic combinations of dual QACs
6th	Polymeric QACs
7th	Bis-QACs with polymeric QACs

ronmental Protection Agency (EPA) is responsible for the registration of all disinfectants. Standardized tests to assess both the bacteriostatic and disinfectant capabilities of products are available (1). This usually includes the testing of both a Gram-negative and a Gram-positive bacterium before the product can be registered. For claims against a specific organism, tests must be conducted with the specific organism to ensure its efficacy.

Numerous studies on QAC efficacy in various applications and against specific organisms have been published. Unfortunately, several neglected to determine if the product had been registered for that specific organism or application. In some cases, purified QACs from a chemical supplier or unidentified source were used rather than formulations designed for a specific organism or application (5), leading to generalized statements that QACs overall are not effective against the target organism. Compounding the problem is the inability of some organisms to grow in the laboratory, requiring the use of surrogates or molecular methods for assessment of product efficacy (6). This has become most evident in the case of norovirus (6).

Norovirus is believed to be the most common cause of foodborne illness in the United States and has caused numerous outbreaks on cruise ships, in hospitals, and in educational institutions (7, 8). Environmental transmission via contaminated hands and fomites is believed to be a major route of transmission (9). Norovirus is also transmitted by contaminated food and water and via aerosols formed from vomit or diarrhea.

Numerous studies on the efficacy of disinfectants against this virus have been conducted (Table 3); mouse norovirus and feline calicivirus are the most commonly used surrogates. The U.S. EPA has used the feline calicivirus for registration of efficacy against human norovirus (10). While mouse norovirus has been shown to be more resistant to some environmental factors and disinfectants than the feline calicivirus is, a meta-analysis of existing studies suggests that the differences are modest (6).

Table 3 lists studies showing formulations registered for norovirus efficacy. When registered QAC formulations were used, efficacy was demonstrated (11, 12). Efficacy is also dependent not only on the target organism(s) but also on the method of application. Bolton et al. compared a hydraulic spray apparatus and a robotic wiping device for sanitizing produce surfaces (11). It was found that the QAC was more effective than chlorine bleach (11) in the spray apparatus but not in the robotic wiping device. This emphasizes that application methods have to be considered in the assessment of any disinfectant.

While numerous laboratory studies on the efficacy of QACs are available (1), relatively few studies have been conducted to assess efficacy in practice. The use of sanitizers is important to reduce the chance of cross contamination of foods during preparation (13). The use of a QAC spray disinfectant in household kitchens was

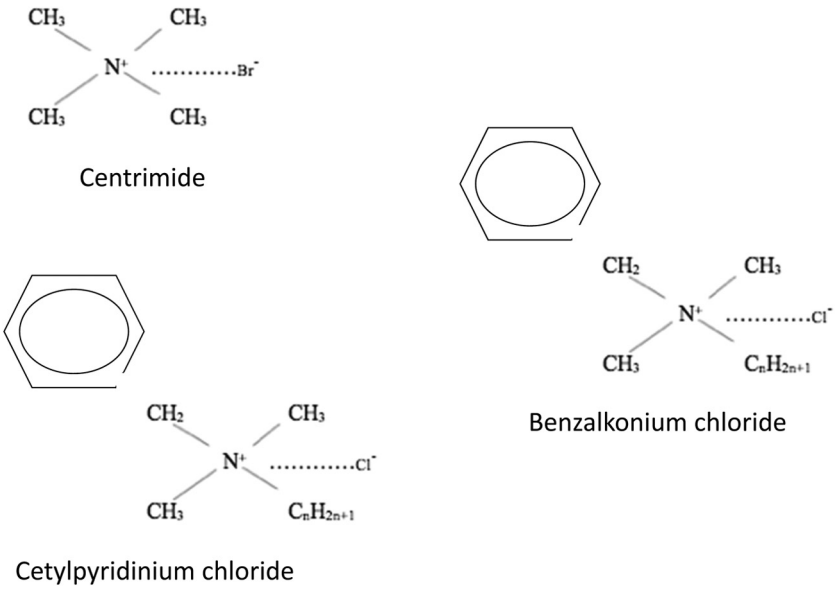

FIG 2 Examples of some common QACs.

TABLE 2 Spectrum of action of QAC formulations against microorganisms

Organism(s)	Reference
Bacteria	
Gram$^+$/Gram$^-$	1
Mycobacterium	41
Bacillus spores	41
Listeria monocytogenes	42
Antibiotic resistant	36
Viruses	
Enteroviruses	36
Rotavirus	43
Norovirus	11
Influenza virus	1
Hepatitis A virus	44
Protozoa	
Acanthamoeba polyphaga (trophozoites)	45
Cryptosporidium parvum	46
Fungus *Trichophyton mentagrophytes* (spores)	41
Algae	1

found to significantly reduce the total numbers of staphylococcal and *Pseudomonas aeruginosa* bacteria (14). No *Salmonella* or *Campylobacter* bacteria were detected after the use of the QAC. Another study in household kitchens and bathrooms found that a QAC wipe reduced total bacterial numbers by 99.9% overall (15). A study involving 30 households in Mexico showed that the use of a QAC product statistically significantly reduced the occurrence of *Escherichia coli* on countertops over the 5 weeks of the study (16). In a study conducted in an elementary school, the use of QAC-based disinfectant wipes once a day on the desk of each student reduced absenteeism by almost 50% (17). During an outbreak of norovirus in a school, a QAC was found not to have stopped virus transmission, but a nonregistered product for norovirus had been used (18).

TABLE 3 Studies on the efficacy of QACs against norovirus

Finding and reference	Product	Norovirus registered[a]	Test virus(es)[b]	Remarks
Not effective				
47	Pinoclean	No	FCV	
48	BAC	No	FCV	Fabrics, carpets[c]
49	Dual QACs	No	MNV, noro	
50	DIDAC, BAC	No	FCV, noro	Stool specimens[c]
51	Oasis 146	No	MNV, noro	
52	Bardac 208 M	No	MNV	
Effective				
12	R-82	Yes	FCV	
53	BAC	?	FCV	Hand rub
54	BAC	?	FCV	
55	BAC	?	FCV	
11	Alpet D2	Yes	MNV	

[a] U.S. EPA, 2009 (10).
[b] FCV, feline calicivirus; MNV, mouse norovirus; noro, human norovirus assessment by molecular methods; BAC, benzalkonium chloride.
[c] QACs are not designed for decontamination of stool specimens or fabrics.

TABLE 4 Factors in QAC selection

Factor	Remarks
Environment	Liquid, fomite, clinical specimen, food surface, product
Organic load	Heavy organic loads may require greater concentrations
Temp	Greater activity at higher temp
Time	Some organisms are inactivated within 2 min; others require ≥10 min
Formulation	QACs have been formulated for specific applications and organisms; these are combinations of QACs or QACs with other ingredients added to enhance efficacy
Concn	Lower concn has a static effect on growth, while higher concn is microbicidal
Target organism	QACs can be formulated for specific applications and target organisms

The method of application of any disinfectant including QACs is important to ensure the proper dosage. For example, the effective dose of the QAC can be compromised by combination with cotton mops and cleaning towels (19, 20). QAC concentrations can be reduced by 50 to 83% by cotton and microfiber cloths (20, 21). Thus, it is important that proper concentrations, as indicated on product labels, be used and monitored. Another option is using disposable disinfecting wipes or other ready-to-use products to deliver an effective concentration of the QAC (15).

The selection of a QAC or any biocide for a particular application requires an understanding of the factors listed in Table 4.

Resistance. The term resistance is used to indicate the insusceptibility of a microorganism to a particular treatment under a given set of conditions. Gilbert and McBain lamented the tendency in the disinfection field to use the term "resistant," even where changes in the dose of disinfectant needed to kill or inhibit the organism was insufficient, resulting in treatment failures (22). Tolerance may be the preferred term to describe any MIC increases, rather than resistance, which implies that the disinfectant can no longer be used for a specific application. It is to be expected that some tolerance among some types of bacteria might occur with the long-term use of QACs. While it is often implied that their continued use will result in the development of resistance, this is not the case. The nonspecific action of QACs makes the development of resistance unlikely (22), and several recent reviews support this conclusion (20, 23–25). The multitarget nature of QACs means that mutation within a single target is unlikely to result in a treatment failure. The MIC increases that occur are much smaller than those seen with antibiotics (26). It has been suggested that rotating different QAC formulations in health care or other settings would reduce this probability, but at this time, there is no evidence that this practice is needed (24). In the home environment, bacteria isolated from sink drains were found to have reduced susceptibility to QACs but no resistance was observed (3).

Because of their low toxicity, QACs are extensively used in food processing and the food service industry. Several recent studies have focused on the potential for the development of resistance among bacterial pathogens. A recent example of this is in the use of QACs to control *Listeria* in the food industry, where several studies have reported the occurrence of *Listeria* resistance to QACs (27, 28). Increases in MICs were reported, but the MICs were still below those used in practice. Differences in the occur-

rence of increased MICs have been reported to vary greatly from food processing plant to food processing plant, but it was suggested that these differences may be due to sublethal disinfectant concentrations or other-less than-optimal hygiene practices (29–31). Kastbjerg and Gram pointed out that while MIC increases are seen in food processing, high acquired tolerance is rare, and that disinfectants are still effective for controlling foodborne pathogens such as *Listeria monocytogenes* (25). In a laboratory study of the impact of disinfectants on the tolerance of *Salmonella* to several different biocides, it was found that there was no development of cross tolerance among the different disinfectants studied, including a QAC (32). It was also found that the increases in tolerance were not phenotypically stable.

A review of resistance to biocides used in the health care industry concluded that there was no clear evidence to support the development of resistance to QACs or other biocides (24). Under in-use conditions, most problems turn out to be related to pseudoresistance or user error, such as overdilution or incorrect handling of the product (20, 23, 24).

Cross-resistance to antibiotics. Efflux pumps act to exclude substances damaging to the microbial cell. Efflux pumps can be induced by many substances besides biocides or antibiotics, including common household chemicals and natural products (26). In some cases, efflux pumps account for the resistance of bacteria to certain antibiotics. Thus, it has been suggested that activation of efflux pumps by biocides enhances antibiotic resistance in bacteria (30, 33).

Studies examining the use of biocides and antibiotic resistance in household drains and in the health care environment and in industry have not observed any antibiotic-resistant bacteria in greater numbers in areas where biocides had been employed than in areas where they had not been used (34).

Several studies have shown no relationship between antibiotic resistance and the use of disinfectants (including QACs) in the home (35–37). In one study, samples of fomites in the kitchen and bathroom were collected from homes that used disinfectants and those that did not. No antibiotic cross-resistance was shown in the target bacteria recovered from the homes of disinfectant product users and nonusers (38). For Gram-positive bacteria resistant to one or more antibiotics, the greatest number was found in the nonuser group. It was also observed that while antibiotic multiresistance was common in households, there was no significant difference between homes that used disinfectants (including QACs) and those that did not.

The American Medical Association has called for the removal of agents in hygiene cleaning products that have exhibited induction of antibiotic resistance, and European regulations have suggested restricting the use of numerous active substances (39). Current evidence does not appear to justify such action. Lack of testing protocols and a definition of the minimal disinfectant concentration that affects antibiotic resistance for a defined strain are not established at present. Clearly, quantitative-risk-based approaches, such as those recently suggested by Ashbolt et al., are needed before any recommendations for limitations on the use of biocides important in reducing exposure to pathogens are considered (40).

CONCLUSIONS

In conclusion, it is important to recognize that many factors have to be considered carefully in selecting a QAC or any other disinfectant or sanitizer. Every QAC formulation has its advantages and disadvantages for a particular situation. Selecting formulations registered for a particular pathogen is crucial. It is also important to recognize that observed effects in laboratory studies of small increases in tolerance to some QAC formulations and association with antibiotic resistance have to be balanced against the benefits to public health from their use. QAC chemistry is a continually evolving area, with new product formulations appearing in the market to meet challenges posed by emerging pathogens. Appropriate use of QACs in food processing and food service, schools, health care facilities, and the home can significantly impact health by reducing the number of infections. Better standardized tests for assessing and defining the differences between increases in tolerance versus resistance are needed. The ecological dynamics of microbial communities where QACs are a main line of defense against exposure to pathogens need to be better understood in terms of sublethal doses and antibiotic resistance. At this time, there appears to be no reason for the restricted use of QACs based on increases in tolerance or induction of efflux pumps.

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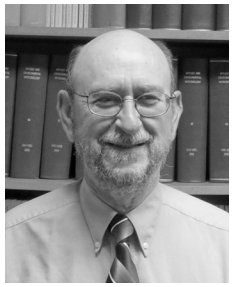
REFERENCES

1. **Merianos JJ.** 2001. Surface-active agents, p 63–320. *In* Block SS (ed), Disinfection, sterilization, and preservation. Lippincott Williams & Wilkins, Philadelphia, PA.
2. **McDonnell GE.** 2007. Antisepsis, disinfection, and sterilization. ASM Press, Washington, DC.
3. **Moore LE, Ledder RG, Gilbert P, McBain AJ.** 2008. In vitro study of the effect of cationic biocides on bacterial population dynamics and susceptibility. Appl Environ Microbiol **74:**4825–4834. http://dx.doi.org/10.1128/AEM.00573-08.
4. **Zinchenko AA, Sergeyev VG, Yamabe K, Murata S, Yoshikawa K.** 2004. DNA compaction by divalent cations: structural specificity revealed by the potentiality of designed quaternary diammonium salts. Chembiochem **5:**360–386. http://dx.doi.org/10.1002/cbic.200300797.
5. **Eterpi M, McDonnell G, Thomas V.** 2009. Disinfection efficacy against parvoviruses compared with reference viruses. J Hosp Infect **73:**64–70. http://dx.doi.org/10.1016/j.jhin.2009.05.016.
6. **Hoelzer K, Fanaselle W, Pouillot R, Van Doren JM, Dennis S.** 2013. Virus inactivation on hard surfaces or in suspension by chemical disinfectants: systematic review and meta-analysis of norovirus surrogates. J Food Prot **76:**1006–1016. http://dx.doi.org/10.4315/0362-028X.JFP-12-438.
7. **Gerba CP, Kayed D.** 2003. Caliciviruses: a major cause of foodborne illness. J Food Sci **68:**1136–1137. http://dx.doi.org/10.1111/j.1365-2621.2003.tb09614.x.
8. **Harris JP, Lopman BA, O'Brien SJ.** 2010. Infection control measures for norovirus: a systematic review of outbreaks in semi-enclosed settings. J Hosp Infect **74:**1–9. http://dx.doi.org/10.1016/j.jhin.2009.07.025.
9. **Lopman B, Gastanaduy P, Park GW, Hall AJ, Parashar UD, Vinje J.** 2012. Environmental transmission of norovirus gastroenteritis. Curr Opin Virol **2:**96–102. http://dx.doi.org/10.1016/j.coviro.2011.11.005.
10. **United States Environmental Protection Agency.** 9 January 2009. List G: EPA's registered antimicrobial products effective against norovirus (Norwalk-like virus). Office of Pesticide Programs, United States Environmental Protection Agency, Washington, DC. http://www.epa.gov/oppad001/list_g_norovirus.pdf. Accessed 18 March 2014.
11. **Bolton SL, Kotwal G, Harrison MA, Law E, Harrison JA, Cannon JL.** 2013. Sanitizer efficacy against murine norovirus, a surrogate for human norovirus, on stainless steel surfaces when using three application methods. Appl Environ Microbiol **79:**1368–1377. http://dx.doi.org/10.1128/AEM.02843-12.

12. **Jimenez L, Chiang M.** 2006. Virucidal activity of a quaternary ammonium compound disinfectant against feline calicivirus: a surrogate for norovirus. Am J Infect Control **34:**269–273. http://dx.doi.org/10.1016/j.ajic.2005.11.009.
13. **Scott E, Bloomfield SF, Barlow CG.** 1982. An investigation of microbial contamination of the home. J Hyg (Lond) **89:**193–203.
14. **Josephson KL, Rubino JR, Pepper IL.** 1997. Characterization and quantification of bacterial pathogens and indicator organisms in household kitchens with and without the use of a disinfectant cleaner. J Appl Microbiol **83:**737–750. http://dx.doi.org/10.1046/j.1365-2672.1997.00308.x.
15. **Gerba CP, Maxwell S, Sifuentes LY, Tamimi AH.** 2013. Impact of a disinfecting wipe on bacterial contamination in households. Househ Pers Care **8**(3)**:**33–35.
16. **Medrano-Félix A, Martinez C, Castro-del Campo N, Leon-Félix J, Peraza-Garay F, Gerba CP, Chaidez C.** 2011. Impact of prescribed cleaning and disinfectant use on microbial contamination in the home. J Appl Microbiol **110:**463–471. http://dx.doi.org/10.1111/j.1365-2672.2010.04901.x.
17. **Bright KR, Boone SA, Gerba CP.** 2010. Occurrence of bacteria, influenza A and norovirus on elementary classroom surfaces. J Sch Nurs **26:**33–40. http://dx.doi.org/10.1177/1059840509354383.
18. **Marks PJ, Vipond IB, Regan FM, Wedgwood K, Fey RE, Caul EO.** 2003. A school outbreak of Norwalk-like virus: evidence for airborne transmission. Epidemiol Infect **131:**727–736. http://dx.doi.org/10.1017/S0950268803008689.
19. **MacDougall KD, Morris C.** 1 May 2006. Optimizing disinfection application in healthcare facilities. Infect Control Today http://www.infectioncontroltoday.com/articles/2006/05/optimizing-disinfectant-application-in-healthcare.aspx.
20. **Rutala WA, Gergen MF, Weber DJ.** 2007. Microbiologic evaluation of microfiber mops for surface disinfection. Am J Infect Control **35:**569–573. http://dx.doi.org/10.1016/j.ajic.2007.02.009.
21. **Engelbrecht K, Ambrose D, Sifuentes L, Gerba C, Weart I, Koenig D.** 2013. Decreased activity of commercially available disinfectants containing quaternary ammonium compounds when exposed to cotton towels. Am J Infect Control **41:**908–911. http://dx.doi.org/10.1016/j.ajic.2013.01.017.
22. **Gilbert P, McBain AJ.** 2003. Potential impact of increased use of biocides in consumer products on prevalence of antibiotic resistance. Clin Microbiol Rev **16:**189–208. http://dx.doi.org/10.1128/CMR.16.2.189-208.2003.
23. **Weber DJ, Rutala WA, Sickbert-Bennett EE.** 2007. Outbreaks associated with contaminated antiseptics and disinfectants. Antimicrob Agents Chemother **51:**4217–4224. http://dx.doi.org/10.1128/AAC.00138-07.
24. **Meyer B, Cookson B.** 2010. Does microbial resistance or adaptation to biocides create a hazard in infection prevention and control? J Hosp Infect **76:**200–205. http://dx.doi.org/10.1016/j.jhin.2010.05.020.
25. **Kastbjerg VG, Gram L.** 2012. Industrial disinfectants do not select for resistance in *Listeria monocytogenes* following long term exposure. Int J Food Microbiol **160:**11–15. http://dx.doi.org/10.1016/j.ijfoodmicro.2012.09.009.
26. **Gilbert P, Allison DG, McBain AJ.** 2002. Biofilms *in vitro* and *in vivo*: do singular mechanisms imply cross-resistance. J Appl Microbiol **92:**98S–110S. http://dx.doi.org/10.1046/j.1365-2672.92.5s1.5.x.
27. **Holah JT, Taylor JH, Dawson DJ, Hall KE.** 2002. Biocide use in the food industry and the disinfectant resistance of persistent strains of *Listeria monocytogenes* and *Escherichia coli*. J Appl Microbiol **92**(Suppl)**:**111S–120S. http://dx.doi.org/10.1046/j.1365-2672.92.5s1.18.x.
28. **Ortiz S, Lopez V, Martinez-Suarez JV.** 2014. Control of *Listeria monocytogenes* contamination in an Iberian pork processing plant and selection of benzalkonium chloride-resistant strains. Food Microbiol **39:**81–88. http://dx.doi.org/10.1016/j.fm.2013.11.007.
29. **Heir E, Lindstedt BA, Rotterud OJ, Vardund T, Kapperud G, Nesbakken T.** 2004. Molecular epidemiology and disinfectant susceptibility of *Listeria monocytogenes* from meat processing plants and human infections. Int J Food Microbiol **96:**85–96. http://dx.doi.org/10.1016/j.ijfoodmicro.2004.03.014.
30. **Ortega Morente E, Fernández-Fuentes MA, Grande Burgos MJ, Abriouel H, Pérez Pulido R, Gálvez A.** 2013. Biocide tolerance in bacteria. Int J Food Microbiol **162:**13–25. http://dx.doi.org/10.1016/j.ijfoodmicro.2012.12.028.
31. **Fernandez-Fuentes MA, Morente EO, Hikmate A, Pulido RP.** 2012. Isolation and identification of bacteria from organic foods: sensitivity to biocides and antibiotics. Food Control **26:**73–78. http://dx.doi.org/10.1016/j.foodcont.2012.01.017.
32. **Condell O, Iverson C, Cooney S, Power KA, Walsh C, Burgess C, Fanning S.** 2012. Efficacy of biocides used in the modern food industry to control *Salmonella enterica*, and links between biocide tolerance and resistance to clinically relevant antimicrobial compounds. Appl Environ Microbiol **78:**3087–3097. http://dx.doi.org/10.1128/AEM.07534-11.
33. **Weber DJ, Rutala WA.** 2006. Use of germicides in the home and healthcare setting: is there a relationship between germicide use and antibiotic resistance? Infect Control Hosp Epidemiol **27:**1107–1119. http://dx.doi.org/10.1086/507964.
34. **Russell AD.** 2003. Biocide use and antibiotic resistance: the relevance of laboratory findings to clinical and environmental situations. Lancet Infect Dis **3:**794–803. http://dx.doi.org/10.1016/S1473-3099(03)00833-8.
35. **Rutala WA, Barbee SL, Aguiar NC, Sobsey MD, Weber DJ.** 2000. Antimicrobial activity of home disinfectants and natural products against potential human pathogens. Infect Control Hosp Epidemiol **21:**33–38. http://dx.doi.org/10.1086/501694.
36. **Rutala WA, Weber DI, Barbee SL, Gergen MF, Sobsey MD.** 2000. Evaluation of antibiotic resistant bacteria in home kitchens and bathrooms. Infect Control Hosp Epidemiol **21:**132.
37. **Cole EC, Addison RM, Rubino RM, Leese KE, Dulaney PD, Newell MS, Wilkins J, Gaber DJ, Wineinger T, Criger DA.** 2003. Investigation of antibiotic and antibacterial agent cross-resistance in target bacteria from homes of antibacterial product users and nonusers. J Appl Microbiol **95:**664–676. http://dx.doi.org/10.1046/j.1365-2672.2003.02022.x.
38. **Marshall BM, Robleto E, Dumont T, Levy SB.** 2012. The frequency of antibiotic-resistant bacteria in homes differing in their use of surface antibacterial agents. Curr Microbiol **65:**407–415. http://dx.doi.org/10.1007/s00284-012-0172-x.
39. **Buffet-Bataillon S, Tattevin P, Bonnaure-Mallet M, Jolivet-Gougeon A.** 2012. Emergence of resistance to antibacterial agents: the role of quaternary ammonium compounds—a critical review. Int J Antimicrob Agents **39:**381–389. http://dx.doi.org/10.1016/j.ijantimicag.2012.01.011.
40. **Ashbolt NJ, Amezquita A, Backhaus T, Borriello P, Brandt KK, Collignon P, Coors A, Finley R, Gaze WH, Heberer T, Lawrence JR, Larsson DGJ, McEwen SA, Ryan JJ, Schonfeld J, Silley P, Snape JR, Van den Eede C, Topp E.** 2013. Human health risk assessment (HHRA) for environmental development and transfer of antibiotic resistance. Environ Health Perspect **121:**993–1001. http://dx.doi.org/10.1289/ehp.1206316.
41. **Best M, Springthorpe VS, Sattar SA.** 1994. Feasibility of a combined carrier test for disinfectants: studies with a mixture of five types of microorganisms. Am J Infect Control **22:**152–162. http://dx.doi.org/10.1016/0196-6553(94)90004-3.
42. **Fazlara A, Ekhtelat M.** 2012. The disinfection effects of benzalkonium chloride on some important food borne infections. Am-Eurasian J Agric Environ Sci **12:**23–29.
43. **Bosch A.** 1998. Human enteric viruses in the water environment: a minireview. Int Microbiol **1:**191–196.
44. **Mbithi JN, Springthorpe S, Sattar SA.** 1990. Chemical disinfection of hepatitis A virus on environmental surfaces. Appl Environ Microbiol **56:**3601–3604.
45. **Vaerewijck MJM, Sabbe K, Bare J, Spengler HP, Favoreel H, Houf K.** 2012. Assessment of the efficacy of benzalkonium chloride and sodium hypochlorite against *Acanthamoeba polyphaga* and *Tetahymena* spp. J Food Prot **76:**541–546. http://dx.doi.org/10.4315/0362-028X.JFP-11-359.
46. **Thomas V.** 2013. Sensitivity and resistance of protozoa to biocides, p 155–177. *In* Fraise A, Mailard JV, Sattar S. (ed), Russell, Hugo and Ayliff's principals and practice of disinfection, preservation and sterilization. Wiley, New York, NY.
47. **Doultree JC, Druve JD, Birch CJ, Bowden DS, Marshall JA.** 1999. Inactivation of feline calicivirus, a Norwalk virus surrogate. J Hosp Infect **41:**51–57. http://dx.doi.org/10.1016/S0195-6701(99)90037-3.
48. **Malik YS, Allwood PB, Hedberg CW, Goyal SM.** 2006. Disinfection of fabrics and carpets artificially contaminated with calicivirus: relevance in institutional and healthcare centres. J Hosp Infect **63:**205–210. http://dx.doi.org/10.1016/j.jhin.2006.01.013.
49. **Girard M, Ngazoa S, Mattison K, Jean J.** 2010. Attachment of noroviruses to stainless steel and their inactivation, using household disinfectants. J Food Prot **73:**400–404.
50. **Nowak P, Topping JR, Fotheringham V, Gallimore CI, Gray JJ, Iturriza-Gomara M, Knight AI.** 2011. Measurement of the virolysis of human GII.4 norovirus in response to disinfectants and sanitizers. J Virol Methods **174:**7–11. http://dx.doi.org/10.1016/j.jviromet.2011.03.004.
51. **Feliciano L, Li J, Lee J, Pascall MA.** 2012. Efficacies of sodium hypochlorite and quaternary ammonium sanitizers for reduction of norovirus and

selected bacteria during ware-washing operations. PLoS One 7(12): e50273. http://dx.doi.org/10.1371/journal.pone.0050273.
52. **Tung G, Macinga D, Arbogast J, Jaykus L.** 2013. Efficacy of commonly used disinfectants for inactivation of human noroviruses and their surrogates. J Food Prot **76:**1210–1217. http://dx.doi.org/10.4315/0362-028X.JFP-12-532.
53. **Mori K, Hayashi Y, Akiba T, Noguchi Y, Yoshida Y, Kai A, Yamada S, Sakai S, Hara M.** 2007. Effects of hand hygiene on feline calicivirus inactivation and removal as norovirus surrogate treated with antiseptic hand rubbing, wet wipes and functional water. Kansenshogaku Zasshi **81:**249–255. (In Japanese.)
54. **Whitehead K, McCue KA.** 2010. Virucidal efficacy of disinfectant actives against feline calicivirus, a surrogate for norovirus, in a short contact time. Am J Infect Control **38:**26–30. http://dx.doi.org/10.1016/j.ajic.2009.03.015.
55. **Su X, D'Souza DH.** 2012. Inactivation of human norovirus surrogates by benzalkonium chloride, potassium peroxymonosulfate, tannic acid, and gallic acid. Foodborne Pathog Dis **9:**829–834. http://dx.doi.org/10.1089/fpd.2012.1155.



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