

Antimicrobial products in the home: The evolving problem of antibiotic resistance

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Antimicrobial agents are increasingly being incorporated into a wide variety of products for use in the home [1][2]. Principles for the judicious use of antibiotics for common paediatric infections have been published and reviewed [3]. However, similar principles have not been established for antimicrobial products that are used in the home. The present position statement examines the risks and benefits of the use of antimicrobial products in the home and outlines appropriate home hygiene measures for common scenarios.

Types of antimicrobial products in the home

Antimicrobial chemicals (biocides) include sterilants, disinfectants and fungicides. Biocides are generally synthetic or semisynthetic molecules that, above certain concentrations and under defined conditions, will kill living cells within specified time intervals. Sterilants destroy all forms of microbial life; disinfectants eliminate infectious pathogenic bacteria; sanitizers reduce microbial contaminants; and fungicides destroy fungi on inanimate surfaces that are pathogenic to humans and animals.

Mechanical devices are sometimes used to control microorganisms in indoor air, including electronic air cleaners, ion generators, mechanical filters, pleated (eg, high-efficiency particulate air) filters, activated charcoal impregnated filters, ozone generators, ultraviolet light and thermal mechanisms.

Impregnated devices include a wide variety of domestic products, such as clothes (eg, undergarments, sporting garments and jeans), toys, kitchen utensils and a wide variety of plastic products. Additional products include antimicrobial window

cleaners, antimicrobial chopsticks and bed clothing (eg, pillows, sheets, towels and slippers) in some countries [2].

The active ingredients in the above types of products vary from alcohols, peroxides and halides to antimicrobial chemicals, such as triclosan and quaternary ammonium compounds.

Alcohols

Alcohol-based hand antiseptics contain isopropanol, ethanol or n-propanol, alone or in combination [4]. Alcohols denature proteins, which is believed to be the main mechanism of antimicrobial action. Solutions containing 60% to 95% alcohol are most effective. The antimicrobial action of alcohols is transient but the effects may be prolonged by the addition of other chemicals, such as chlorhexidine or triclosan. Alcohols have a wide spectrum of activity, but are less active against bacterial spores, some nonenveloped (nonlipophilic) viruses and protozoan oocysts. Alcohol-based hand rubs do have activity against several nonenveloped viruses (eg, rotavirus, adenovirus, rhinovirus, hepatitis A and poliovirus). However, alcohol may not be effective against hepatitis A and other nonlipophilic viruses, depending on the alcohol concentration and the amount of time that viruses are exposed to the alcohol.

Chlorhexidine

Chlorhexidine gluconate is a cationic bisbiguanide [4]. The mechanism of action is believed to be the disruption of cytoplasmic membranes with subsequent precipitation of cellular material. Chlorhexidine gluconate is active against Gram-positive bacteria, is less active against Gram-negative bacteria and fungi, and only exhibits minimal activity against *Mycobacterium tuberculosis*. It is not sporicidal and

has in vitro activity against enveloped viruses (eg, herpes simplex virus, HIV, cytomegalovirus, influenza and respiratory syncytial virus), but has less activity against nonenveloped viruses (eg, rotavirus, adenovirus and enteroviruses). Chlorhexidine gluconate is included in a number of hand hygiene preparations and antiseptic detergent preparations.

Triclosan

Triclosan is a nonionic substance that has been incorporated into soaps and other consumer products [4]. Concentrations of 0.2% to 2% have antimicrobial activity. Triclosan enters bacterial cells and affects the cytoplasmic membrane and synthesis of RNA, fatty acids and proteins. It has a broad range of antimicrobial activity. It is often bacteriostatic. Triclosan's activity against Gram-positive organisms is greater than against Gram-negative bacilli. The agent possesses reasonable activity against mycobacteria and Candida species, but it has limited activity against filamentous fungi. Like chlorhexidine, the activity of triclosan on the skin is more persistent than that of alcohol.

Quaternary ammonium compounds

The antimicrobial activity of quaternary ammonium compounds is likely attributable to their adsorption onto the cytoplasmic membrane, with subsequent leakage of low molecular weight cytoplasmic components [4]. Quaternary ammonium compounds are mainly bacteriostatic and fungistatic, although they are microbicidal against certain organisms at high concentrations. They are more active against Gram-positive bacteria than against Gram-negative bacilli. These compounds are active against lipophilic viruses, but they are less active against mycobacteria and fungi. Among these compounds, benzalkonium chlorides are the most frequently used.

Other compounds

There are several antimicrobial agents that may be used alone or in combination. Some of these, such as chlorine-based and iodine-based products, are well established as being very useful in specific situations (eg, dilute bleach is recommended for cleaning up spillage of body fluids) [4]. Chloroxylenol (parachlorometaxyleneol or PCMX) is used as a preservative in cosmetics and other products, and is also used in antimicrobial soaps [4].

Facial tissue impregnated with an antiviral agent has been promoted. The first of these tissues to be commercially available is Kleenex (Kimberly-Clark,

USA) [5]. The tissue has three layers, with a moisture-activated middle layer. This layer contains citric acid and sodium lauryl sulfate, which are active against rhinoviruses and several enveloped viruses, respectively. The product is virucidal in vitro against rhinoviruses type 1A and type 2, influenza A and influenza B, and respiratory syncytial virus. However, virus that is transferred from nose to tissue without passing through the active layer is still infectious. It has not been established whether this product can reduce transmission of respiratory infections in households. It has been suggested that frequent handwashing may be more effective [5].

Real-life effectiveness of antimicrobial products

The in vitro activity of some specific products is addressed above. The value of some agents for specific uses has been well established (eg, bleach and alcohols). The use of dilute bleach is recommended for cleaning up significant spillage of body fluids. Alcohol-based solutions and gels may be used for washing hands if soap and water are not available. With respect to other bacterial products, varying degrees of effectiveness have been demonstrated in suspension tests in vitro [6][7]. In one study [6], the effects of an antibacterial dishwashing liquid on *Escherichia coli*, *Salmonella enteritidis*, *Staphylococcus aureus* and *Bacillus cereus* were investigated in a modified suspension test and in used sponges with and without food residues, under laboratory conditions. The investigators also conducted tests in households to assess the efficacy of antibacterial dishwashing liquid. The results demonstrated that the antibacterial dishwashing liquid was effective in reducing pathogens in the laboratory-based suspension test but not in the used sponges in the real household setting. This finding suggested that to determine the efficacy of antibacterial products, their use in real-life settings must be evaluated. The effectiveness of antibacterial agents was evaluated in one recently conducted randomized controlled trial [7]. In this trial, Larsen et al [7] studied two sets of households from Manhattan, assigning 120 household (552 persons) to agents containing antibacterial agents. The control group (118 households, 586 persons) received identically packaged agents without antibacterial properties. Antibacterial activity was defined by the presence of triclosan, quaternary ammonium compounds, hypochlorite or other recognizable microbicidal agents in concentrations

greater than preservative levels. No differences in episodes of infectious diseases were found.

Thus, while in vitro activity of various products has been demonstrated, effectiveness in real-life household settings is lacking and is not supported by data from the only randomized trial on the subject.

Antimicrobial resistance

Mechanisms of antimicrobial resistance and reduced susceptibility to biocides

Microorganisms have evolved mechanisms that enable them to evade the action of antimicrobials. Several different mechanisms of resistance have been described in bacteria [8]. These include the following: enzymatic inhibition, membrane impermeability, efflux pumps, alteration of the ribosomal target, alteration of the cell wall precursor target, alteration of target enzymes, overproduction of target enzymes and auxotrophs that bypass inhibited steps. While some of these mechanisms apply to biocides in theory, this is less well studied. Where simultaneous changes in susceptibility to antibiotics and biocides occur, the determinants of resistance have mostly involved genes that encode for multidrug efflux pumps. These genes may be plasmid-borne in Gram-positive species or chromosomally encoded in Gram-negative species [9].

Examples of biocide use and reduced susceptibility

Triclosan-resistant mutants of *E coli*, *S aureus* and other organisms have been isolated in the laboratory [9]-[11]. The use of triclosan may potentially enhance the growth of resistant strains of *Streptococcus pneumoniae* and *Enterococcus faecalis* [2]. This has raised concerns regarding the effect of home use of residue-producing biocides on the microbiology of the home and on the long-term effectiveness of biocides. While the development of reduced susceptibility to biocides in response to biocide exposure can occur, in the short-term, it is not likely that this would compromise the effectiveness of these agents in situations where much higher concentrations are used. However, the long-term consequences of continued biocide use and emerging resistance are less clear. One concern is not just related to the effectiveness of the biocide, but to the potential for cross-resistance to important antibiotics [10].

Potential links between biocide use and antibiotic resistance

Concern has been expressed regarding whether biocide use contributes to antibiotic resistance [10][12]. Data by Levy [10] showed the occurrence of triclosan-resistant *E coli* strains that emerged with low-, medium- and high-level resistance. All the mutants were in a single gene (*fab1*) that codes for an enzyme in fatty acid biosynthesis. This gene also produces resistance to other structurally unrelated antimicrobials, such as isoniazid. The investigator demonstrated that triclosan-resistant mutant strains of *Mycobacterium smegmatis* were also resistant to isoniazid [13]. *M smegmatis* showed cross-resistance to both drugs regardless of whether the resistant mutants were selected out by triclosan or isoniazid. To date, this cross-resistance has not been shown for isoniazid-resistant strains of *Mycobacterium tuberculosis*.

Laboratory-based evidence suggests that strains of *E coli* with efficient efflux pumps may be selected out by antibacterial agents, such as the disinfectant pine oil [14]. Mutations that upregulate efflux pumps may cause antibiotics to be pumped out efficiently, so that the drugs do not regain entry into the bacterial cell. Multidrug-resistant efflux pumps are often nonspecific, thereby enabling the bacterium to pump out several different antibiotics and antibacterial chemicals [15]. Thus, in theory, the upregulation of efflux pumps by an agent such as pine oil could lead to resistance to several antibiotics.

Some experts have expressed concern that the widespread use of surface antimicrobial agents may help to explain the appearance of a different kind of methicillin-resistant *S aureus* (MRSA) in some communities [2]-[10]. This type of MRSA exhibits resistance that is limited to beta-lactams, unlike the hospital MRSA strains that are usually resistant to many drugs. It has been suggested that the use of antibacterials in the home may provide a selective advantage to less dominant organisms, such as MRSA. Japanese researchers have been able to use benzalkonium chloride to select mutants of MRSA that exhibit antibiotic susceptibility patterns that are similar to community-acquired strains of MRSA. Such MRSA strains exhibited resistance to methicillin, some cephalosporins and penicillins [15]. Chlorhexidine- and triclosan-resistant strains of MRSA have been described [16][17]. However, the clinical significance is unclear, and this has not been shown to correlate with a specific corresponding pattern of antibiotic resistance [17]. Likewise, with respect to another Gram-positive

organism, *Streptococcus mutans*, a study [18] of school children and students from families in which 70% regularly used oral preparations of chlorhexidine showed no evidence of resistance to chlorhexidine or to a range of antibiotics.

In summary, there is no definitive evidence that the use of biocides has contributed to the development of antibiotic resistance either in clinical practice or in the general environment [9]. However, there are relationships between antibiotic resistance and biocides that are mediated by a target gene mutation or increased expression of multidrug efflux pumps. Consequently, the potential impact of biocides on antibiotic resistance requires continued scrutiny.

Link between antibacterial products and allergies

Many experts believe that for normal maturation, the immune system must be stimulated to acquire the precise balance between T helper (Th)-1 and Th-2 activity. Individuals with allergies and eczema are more likely to have a Th-1:Th-2 imbalance, with more Th-2 activity. Some experts are concerned that there may be an association between too much hygiene and allergies [19]-[21]. It has been speculated that if there is an association between infections in early childhood and a decreased incidence of allergies and asthma [22], it is possible that the excessive use of antibacterials in the home may predispose children to the development of allergies and asthma.

Controlling infections in the home

The desire by families to seek out various antibacterial products often represents a sincere desire to cope with the various scenarios that may be associated with the transmission of infectious organisms in the home. In the section below, we have outlined common situations that are encountered in the home and the appropriate hygiene strategies to deal with them.

Hygiene of the skin

Skin hygiene for health care professionals and the general public has been recently addressed [23][24]. Cleansing with an antimicrobial product reduces rates of cutaneous infection and may be beneficial when skin infections are likely or before certain surgical procedures [23]. However, current data do not support a

recommendation for routine bathing with antimicrobial products.

It is difficult to make a single recommendation regarding hand hygiene practices in the home as it relates to the use of antimicrobial products. However, in general, mild, plain soaps are sufficient for the overwhelming majority of domestic uses. Waterless hand hygiene solutions and gels are a proven alternative to traditional handwashing agents. Because hands are a primary mode of fecal-oral and respiratory transmission of organisms, specific indications for the use of antiseptic hand products may include immediate close contact with persons at high risk for infection, such as those who care for neonates, very old persons and immunocompromised persons in the home. In these situations, one may use an approach that is modified from what is done in health care settings [25] [26].

Respiratory tract infections

The primary means by which illnesses such as colds and influenza spread is from person to person via respiratory droplets or by direct contact with articles recently contaminated by respiratory secretions. Contaminated hands are an efficient means by which infection can be transmitted, with viral particles being deposited in the mouth, nose or eyes. Frequent handwashing and not sharing items such as cups, glasses and utensils with persons who have a respiratory tract illness should decrease the spread of virus to others. These respiratory illnesses include influenza and respiratory syncytial virus infection. In general, a 15 s to 20 s handwash is recommended. If regular soap and water are not available, alcohol-based gel sanitizers or disposable hand wipes may be used.

Coughing and sneezing

Coughing and sneezing should be done into a tissue, which is then discarded. One should cover his or her cough or sneeze if a tissue is not immediately available. In these situations, the hands should be cleaned afterward.

Diarrhea and vomiting

Persons can reduce their chances of getting or transmitting infection by frequent handwashing, especially after changing diapers. In addition, there should be prompt disinfection of contaminated surfaces with household chlorine bleach-based cleaners, as well as prompt washing of soiled articles of clothing.

Handling spills

Body fluids, such as blood, feces and vomit, may be potentially contaminated with different kinds of organisms. Spills in the home or related environs, such as the pool deck, should be cleaned up and the contaminated surfaces disinfected as soon as possible. While there are several available disinfectants, regular household bleach is commonly used. The recipe consists of nine parts water and one part bleach. Disposable gloves should be used to prevent contamination of the hands. The following procedure is recommended:

- Wipe up the spill using paper towels or absorbent material and place in a plastic garbage bag.
- Gently pour bleach solution onto all contaminated areas of the surface.
- Let the bleach solution remain on the contaminated area for 20 min.
- Wipe up the remaining bleach solution.
- Disinfect all nondisposable cleaning materials used, such as mops and scrub brushes, by saturating them with bleach solution and allowing them to air dry.
- Remove gloves and place in plastic garbage bags with all soiled cleaning materials.
- Double-bag and securely tie up plastic garbage bags, and discard.
- Thoroughly wash hands with soap and water.

Controlling cross-contamination in the kitchen

Cross-contamination in the home kitchen may be controlled with the combination of safe food handling practices, handwashing and drying, cleaning and disinfection practices. Cleaning and disinfection can be achieved using soap and detergents, heat, drying, the mechanical action of dishwashers and the selective use of disinfectants. The latter may be used for the decontamination of fixed food surfaces that cannot be taken to the kitchen sink. In such situations, a reliable commercial kitchen disinfectant or a dilute bleach solution may be used. Surfaces such as counters and cutting boards that are specially impregnated with antimicrobial agents are not recommended for use in the kitchen. Surfaces that are damaged and scratched can be difficult to clean and should be replaced.

Cleaning toys in the home

It is not necessary to purchase toys that are impregnated with antimicrobial agents. It is preferred that toys that are placed in children's mouths or otherwise contaminated by body secretions be cleaned with water and detergent, disinfected and rinsed before handling by another child ^{[25][26]}. Alternatively, plastic toys that are machine-washable can be cleaned using the dishwasher. Machine-washable cloth toys can be cleaned using the clothes washing machine. Other types of toys that require cleaning by hand may be cleaned with soap and water or dilute bleach solution.

Carpets and rugs

Carpets and rugs should be vacuumed and cleaned regularly. In addition to routine vacuuming, carpets in infant areas should be cleaned at least monthly, and at least every three months in other areas and when soiled ^[26]. Smaller rugs can be shaken outdoors or vacuumed ^[26].

Recommendations

- The Canadian Paediatric Society does not recommend the use of antimicrobial-impregnated household products. In many situations, the use of antiseptics and antimicrobials is unnecessary.
- The Canadian Paediatric Society promotes hand hygiene using plain soap and water in the vast majority of domestic settings.
- Alcohol-based solutions or gels can be used to wash hands if regular soap and water are not available. Such alcohol-based products should be kept out of the reach of young infants and children.
- Antimicrobial chemical agents may be used selectively in the home in specific high-risk scenarios, such as the care of individuals who are receiving medical care at home.
- Where appropriate, alcohol, bleach or peroxidase-based agents are preferred because they dissipate readily and are less likely to exert prolonged antimicrobial pressure. Agents such as triclosan, chlorhexidine and quaternary ammonium compounds exert more prolonged antimicrobial pressure.
- Health care personnel should encourage educational strategies that minimize the risk of transmission of infections in the home.

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