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The Effect of Strict Infection Control Strategies on the Rate of Antibiotic Resistance Bacteria

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Abstract

Introduction: Because interhospital variation in susceptibility patterns may be substantial, hospitals should be cautious when extrapolating infection control data or data from other hospitals to their particular institution. Hence, this review aims to highlight the effect of strict infection control strategies on the rate of antibiotic resistance bacteria.

Methods: Articles were identified by searching MEDLINE and Current Contents. The search was limited to English language articles published till 2022. We used the search terms resistance, antibiotics, nosocomial, infection, and intensive care. Eligible articles presented at these meetings were included if they were available for review and had been accepted for publication in a peer-reviewed medical journal.

Results: The threat of antimicrobial resistance (AMR) is growing at an alarming rate and the situation is perhaps aggravated in developing countries due to gross abuse in the use of antimicrobials . It is well known that any use of antimicrobials however appropriate and justified, contributes to the development of resistance, but widespread unnecessary and excessive use makes the situation worse. Misuse of antimicrobials is facilitated in developing countries by their availability over the counter, without prescription and through unregulated supply chains. Non-compliance in the use of antimicrobials has many repercussions upon resistance and poverty is a major root factor of antimicrobial misuse in developing countries.

Conclusions: Self-medication is a common practice in developing countries where patients often get antimicrobials without prescription and through unregulated supply chains These actions result in the exposure of surviving pathogens to sub-therapeutic concentrations of antimicrobials thus increasing the chances of acquiring resistance.

Keywords: ***Antibiotic misuse, Resistance, Bacteria, Hospitals.***

Introduction

An increasing prevalence of antibiotic resistance is a major concern in the selection of empiric antibiotic therapy for critically ill intensive care unit (ICU) patients. The development of resistance to antimicrobial agents has been an ongoing and evolving process since antibiotics first were introduced a half century ago [1]. It is a widely held notion that sooner or later bacteria will develop resistance to almost any antimicrobial agent. Compared to infections caused by susceptible strains, infections caused by antibiotic-resistant organisms are more likely to prolong hospitalization, to increase the risk of death, and to require treatment with more toxic or more expensive antibiotics. Inappropriate therapy, including therapy to which a pathogen is resistant, has been identified as an independent risk factor for increased mortality in patients with gram-negative bacteraemia or nosocomial pneumonia, and estimates of the excess hospital costs due to antibiotic resistance range from $100 million to $30 billion annually in US hospitals [2]. Therefore, in this review, we have tried to establish guidelines for avoiding and, when necessary, controlling resistance problems in ICUs. The definition of antibiotic-resistant organisms has evolved with time. No longer are penicillin-resistant staphylococci considered a resistance problem, as they were in the 1950s [3].

Factors that may contribute to the emergence and dissemination of antimicrobial resistance include inadequate infection control, high antimicrobial usage per geographic area per unit time, increased use of antimicrobial prophylaxis, increased empiric polymicrobial antimicrobial therapy, greater severity of illness of hospitalized patients, more severely immunocompromised patients, newer devices and procedures in use, agricultural use of antimicrobials, social factors, international travel, evolution of pathogens [4]. Evidence suggests that a causal factors relationship exists between antimicrobial usage and antimicrobial resistance. For example, hospital wards with high antibiotic utilization have high rates of resistance; changes in antimicrobial usage in such settings are often accompanied by changes in resistance patterns. Also, an increased duration of antimicrobial exposure is accompanied by an increased risk of colonization with resistant organisms. Within the hospital setting, the proportion of patients who are severely ill and/or immunocompromised may also increase the risk of resistance. In recent years, the proportion of hospitalized patient who have advanced malignancies, multiorgan failure, human immunodeficiency virus, and organ transplants has increased greatly. These patients are more likely than the general population to be infected or colonized with organisms that are more resistant to antimicrobials [5]. These patients are also more likely to require procedures and devices that increase the risk of infection. A number of social factors also may affect the rate of antimicrobial resistance. For example, the concentration of very young and very old individuals in a given environment and extensive travel may play a role in the development of resistance. Other risk factors include poverty, malnutrition, poor education, and lack of access to health care [6].

A key component to minimizing the dissemination of antimicrobial resistance is the implementation of effective infection control practices, including hand hygiene, isolation, and surveillance. Although implementation of such practices has proved to be effective in deterring the spread of antimicrobial resistance, some of these practices are not used on a routine basis. Isolation, for example, can be useful in patients colonized with resistant organisms but is not practical in most circumstances. In contrast, hand hygiene is an effective yet simple infection control

practice that is vastly underused [7]. In fact, most studies evaluating compliance with hand hygiene report only a 29-48% compliance rate among health care workers, regardless of discipline. Even when health care professionals are washing their hands, many are not doing so for an adequate duration of time. Data reported by an infection control practices advisory committee and a hand hygiene task force demonstrate, on average, an overall need for improvement in the duration of hand washing by health care workers. Recognizing this need for improvement, the committee and task force issued guidelines that extensively review the importance of hand hygiene and provide numerous recommendations on the subject, including hand hygiene techniques, surgical hand antisepsis, and selection of hand hygiene agents. They also provide the following indications for hand washing and hand antisepsis [8]. In addition to hand hygiene, health care professionals must recognize that organisms may spread through inanimate objects, including stethoscopes and other instruments that clinicians carry. Also, care must be taken when handling any items in the patient' s environment, including clothing, linens, and equipment. surveillance and reporting of resistance patterns are other key components of infection control. All institutions should have policies and procedures for conducting routine surveillance, which consists of a periodic review of minimum inhibitory concentration (MIC) or zone diameter data to detect changes in resistance patterns as indicated by increases in MICs or decreases in zone diameters. Another important part of resistance reporting is providing clinicians with antimicrobial susceptibility testing data on isolates obtained from their individual patients. Finally, evolution of the bacterial pathogens over time clearly contributes to the growing problem of resistance [9].

Now we must deal with endemic methicillin-resistant staphylococci, the increasing resistance of gram-negative bacilli to broad-spectrum ␤-lactam antibiotics, and the emergence of multi-resistant enterococci. One working approach is to define antimicrobial resistance as a problem when it requires clinicians to alter antibiotic therapy substantially either by substituting more toxic or expensive agents or by using more complex multidrug regimens to treat suspected or documented resistant pathogens [10]. Bacteria are extremely adaptive to the challenge of antimicrobial therapy, and they have evolved a variety of resistance mechanisms, including enzymes that inactivate or modify antibiotics, diminished permeability (or increased efflux) of antibiotics, and altered antibiotic target sites (through reduction in receptor affinity or the substitution of an alternative pathway). Resistance may arise as a result of a spontaneous mutation, for example, which reduces target affinity or overrides a repressor gene allowing production of an antibiotic-inactivating enzyme. Resistance genes also may be transferred from other organisms by way of extrachromosomal deoxyribonucleic acid or chromosomal DNA [11].

Although laboratory tests cannot simulate the complex in vivo environment, which is influenced by pharmacokinetic and pharmacodynamic factors and by the patient's immunologic status and underlying conditions, 9 routine susceptibility tests from clinical microbiology laboratories generally are reliable indicators of bacterial resistance, and such in vitro resistance usually correlates with clinical outcome [12]. Certain pitfalls in susceptibility testing should be recognized. For example, many clinical microbiology laboratories use "class" susceptibility testing for In an effort to reduce costs, some microbiology laboratories do not repeat susceptibility testing when the same species is isolated repeatedly from the same source, but instead refer to the susceptibility profile of the initial isolate. Because resistance may emerge rapidly, failure to repeat susceptibility testing on subsequent isolates may result in delayed recognition of resistance and consequent clinical failure [13]. In addition, susceptibility testing is not performed routinely on some organisms unless recovered from normally sterile body sites, so resistance may be missed (eg, vancomycin-resistant enterococci). The problem of antimicrobial resistance is global. Initially, antibiotic resistance may emerge in response to local factors (eg, particular antibiotic use patterns), but once resistance emerges in one geographic area, it often appears in other areas in short order. In part, this can be attributed to the ease with which bacteria exchange genetic information coding for resistance, to lapses in technique that transmit resistant organisms from one patient to another, and probably to the spread of

bacteria within the community and to other communities [14]. The TEM B-lactamase spread from gram-negative bacilli to Hemophilus influenzae and Neisseria gonorrhoeae in the 1970s; more recently, it has appeared in Neisseria meningitidis. A multi-resistant clone of serotype 23F Streptococcus pneumoniae recovered for over a decade in Spain and South Africa now is disseminated in the United States. These isolates demonstrate high-level resistance to penicillin, chloramphenicol, trimethoprim-sulfamethoxazole, and tetracycline and variable resistance to erythromycin and cephalosporins [14].

Among nosocomial pathogens, plasmid-mediated extended-spectrum ␣-lactam resistance in enteric gram-negative bacilli first was described in Europe, especially in ICUs, where third-generation cephalosporins had achieved widespread use earlier than in other parts of the world. Within 5 years, similar resistant nosocomial strains were reported around the world, including several sites in the United States. 30 B-Lactamase enzymes also are spreading among gram-positive bacteria. B-Lactamase-producing enterococci have been recognized increasingly since the early 1980s, and the enzyme appears to have come from staphylococci. Sources both outside and inside the hospital may serve as reservoirs of antimicrobial resistance. [13] Substantial variation in the rates of carriage of resistant bacteria among healthy individuals may occur from one community to another, 31 likely reflecting differences in antibiotic use and sanitation. Nursing homes have been identified as reservoirs of both resistant gram-negative bacilli and MRSA. A community outbreak of MRSA infection in Detroit was attributed to the widespread use of empiric cephalosporins by intravenous drug users. Nevertheless, nosocomial bacteria generally are more antibiotic resistant than community isolates, and isolates from tertiary-care hospitals are more resistant than those from community hospitals. Moreover, based on nosocomial infection data reported to the Center for Disease control and prevention's National Nosocomial Infections surveillance (NNIS) System, there has been an overall shift during the past decade away from more easily treated pathogens (eg Escherichia coli Proteus mirabilis, and Klebsiella pneumoniae) toward more resistant pathogens (enterococci MRSA Pseudomonas aeruginosa Enterobacter species, and Candida albicans) in US hospitals [15]. Because interhospital variation in susceptibility patterns may be substantial, hospitals should be cautious when extrapolating infection control data or data from other hospitals to their particular institution. Hence, this review aims to highlight the effect of strict infection control strategies on the rate of antibiotic resistance bacteria.

Methods

Articles were identified by searching MEDLINE and Current Contents. The search was limited to English language articles published till 2022. We used the search terms resistance, antibiotics, nosocomial, infection, and intensive care. The bibliographies of the identified publications were also checked for potentially eligible studies. Finally, the abstract books for the American Thoracic Society and the Intercedence Conference on Antimicrobial Agents and Chemotherapy meetings were reviewed. Eligible articles presented at these meetings were included if they were available for review and had been accepted for publication in a peer-reviewed medical journal. Level I recommendations are supported by randomized, controlled investigations; level II recommendations are supported by nonrandomized concurrent-cohort investigations and historical-cohort investigations; and level III recommendations are supported by case series. Two of the 3 then reviewed the articles and classified them on the basis of the following 4 criteria: type of quasi-experimental study design used, justification of the use of the design, use of correct nomenclature to describe the design, and recognition of potential limitations of the design.

Results and discussion

In recent years healthcare-associated infection (HCAI) has been recognized as a serious patient safety issue. Increased surveillance efforts have identified their incidence and have demonstrated that many are caused by antimicrobial-resistant organisms. HCAI prevention and control measures include the use of environmental biocides [14]. Different microbial species survive in the inanimate environment over a sufficient period to potentially be transferred between

patients within healthcare settings. Intensified environmental cleaning has been shown to reduce the microbial burden of hand contact surfaces and to be cost-effective. Attempts to assess the quality of cleaning using microbiological criteria have been made. Mere cleaning has been shown to spread microbes from the initial point of contamination throughout the environment, even if innovative microfiber materials have been used [15]. Cleaning could not reduce the proportion of methicillin-resistant Staphylococcus aureus (MRSA) environmental swab samples significantly, something that was achieved with hydrogen peroxide vapor disinfection. Routine surface disinfection, instead of cleaning, has therefore been recommended for defined risk areas in healthcare settings. The effect of routine surface disinfection on reducing the number of HCAIs has been rather more controversial. There are numerous reports on antimicrobial resistance to antibiotics, biocides and indeed cross-and co-resistance between these groups of agents. Resistant bacteria have even been reported to grow in extremely high concentrations of substances that are normally regarded as microbicidal at low concentrations. Outbreaks due to microbial contamination of disinfectants and antiseptics have also been reported [16].

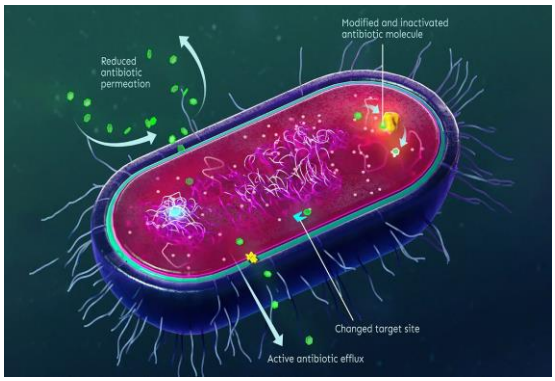
A general reduction in the use of antibiotics is often regarded as necessary in order to reduce selective pressure and the development of resistance against antibiotics. There has been a similar discussion in the field of biocide use concerning preservation, disinfection and antisepsis. Reports on microbial biocide adaptation and resistance have been reviewed previously in this Journal by Russell. To assess their relevance for disinfection in practice the effects have to be classified according to precise definitions. To judge the impact of resistance phenomena on hygiene, clear definitions have to be used and these are absent (or assumed) in much of the literature [17]. Resistance, which is a genetically determined phenomenon, has to be distinguished from phenotypic adaptation processes, which are not inherited or transferable or sustained after the selection pressure is removed. Adaptation to biocides can and should be avoided by rigorous cleaning and disinfection, avoiding concentrations of disinfectants below microbicidal concentration [18]. The European standard EN 14885 gives guidance on standards that disinfectants should pass, to cover defined efficacy spectra. The endpoint for all of these tests is the irreversible destruction of the corresponding test organism. EN 14885 defines a set of test organisms, to evaluate efficacy spectra of biocides, including viruses, vegetative and spore-forming bacteria and fungi. Resistance phenomena are divided into intrinsic and acquired resistance. Intrinsic resistance is the innate greater resistance of certain microbial species compared with others [19]. Mycobacteria, for example, are well-known to be more resistant to biocides than other bacterial species, and bacterial endospores are recognized to be the most biocide-resistant forms of life. These phenomena have to be borne in mind when defining the desired efficacy spectra for disinfectants and disinfection processes. The efficacy spectrum to be selected depends on the susceptibility of patients in that healthcare setting, and the species of pathogenic organisms which are likely to occur there, which can change, for example, during outbreaks [20]. The term 'acquired resistance' is used if certain strains of a microbial species differ significantly (a certain variance in susceptibility to biocides will naturally occur within one species of microbes) in their susceptibility to biocides compared with the average for this species.

When assessing the impact of resistance phenomena on hygiene, it is important to differentiate resistance at the level of minimum microbicidal concentration (MBC) from resistance at the level of minimum inhibitory concentration (MIC). MIC is tested under nutrient-rich conditions, where high concentrations of organic material interfere with the biocidal action of the substance under test. The fact that an organism can grow in nutrient broth with a high concentration of a biocide does not mean that it will survive disinfection [21]. Whereas the level of organic burden used in standard disinfectant testing for the food-processing areas has recently been shown to be representative of situations in practice, no data are available for the healthcare environment. However, the organic soil burden of most surfaces in healthcare settings can be regarded as lower than in food processing. The concentration of organic material in disinfectant solutions will therefore be much lower than in MIC testing [22]. In addition, use-concentrations of disinfectants and antiseptics are usually far above

MIC. We therefore propose the following definition of resistance in the context of disinfection and antisepsis: Resistance is the ability of a microbial strain or species to demonstrate significantly lower microbial reduction than standard test organisms in a treatment that is regarded as microbicidal against the corresponding microbial group according to generally accepted, standardized, quantitative kill tests, e.g. tests defined by EN 14885. Consequently, 'low level resistance' based on MIC determination should explicitly be referred to as 'increased MIC'. Reports based on increased MIC without increased MBC are not considered further in this review evaluating the effect of microbial resistance on hygiene [23]. Finally, when discussing environmental hygiene in healthcare settings, the terms cleaning and disinfection should clearly be differentiated; this is often not done. Cleaning is defined as the removal of visible and invisible dirt.

A certain portion of microbes are removed from a cleaned surface. This literally means that the microbes are not destroyed, but taken to another place, from which they might spread further. Disinfection is defined as the irreversible destruction of microbes which reduces microbial burden of the disinfected surface to a level that renders it safe for a defined purpose [21]. Thus when surfaces are mistakenly stated to have been 'cleaned using chlorine bleach', the term disinfection should be used for this procedure. Antibiotics and biocides have different modes of action. Antibiotics interact very specifically with certain structures or metabolic processes of the microbial cell, such as bacterial ribosomes, specific bacterial enzymes or with bacterial cell wall synthesis. By contrast, the mode of action of biocides is rather unspecific or multifactorial, as summarized by Cloete. They disorganize or puncture biological membranes [e.g. alcohols, quaternary ammonium compounds (QACs), amines] or react non-specifically with functional groups of proteins (e.g. aldehydes, proxygene compounds) or the genetic material (e.g. halogens, aldehydes). Specific mechanisms of action have been reported for triclosan and resistance to this mode of action has been reported Cross-resistance to antibiotics has also been reported, although this mechanism is limited to a low concentration of the substance’s. At typical bactericidal use-concentrations, non-specific membranotropic effects were observed, compromising the functional integrity of the microbial cell membrane [24]. At higher concentrations leakage of intracellular material occurred. From inhibition and kill time studies with several test organisms at different growth phases, it was concluded that the interaction of triclosan with microbial cells is complex and cannot be explained by inhibition of metabolic pathways alone. Destruction of membrane integrity has also been reported for the QAC didecyldimethyl ammonium chloride and benzalkonium chloride. Leakage of potassium from the microbial cell was observed at microbicidal concentrations [25]. The mode of action of cationic biocides has been reviewed by Gilbert and Moore. Although different species of this class of biocides target biological membranes in different ways, the result is non-specific destruction of membrane integrity in all cases.

The same mechanism of action has been demonstrated for an amine derivative. Thus biocides can generally be regarded as acting non-specifically and/or at many cellular target sites at use-concentrations. Many reports on 'resistance' to biocidal substances describe phenotypic adaptation according to the definitions given above. An adaptative response to acidic environments has been reported repeatedly. Its importance for the medical field has also been discussed. Yeasts may be adapted to grow at up to 800 mg/L of sorbic acid, an agent which is used frequently for the preservation of food and cosmetics. However, these researchers did not investigate whether this capacity for growth or survival at higher concentration was lost again during growth in the absence of this chemical [26]. Whereas S. marcescens ATCC 13880 was killed by the recommended use-concentrations of the amphoteric and also by benzalkonium chloride, the resistant strains were not. However, it was not reported whether this tolerance was inherited and stable within these strains (i.e. an acquired resistance by definition) or a phenotypic adaptation (reversible when the agent exposure was removed). Resistances against biocides with mechanisms of action different from surface-active agents have been reported less frequently. Mutoh et al. report an 'adaptive response' of a yeast to hydrogen peroxide, which has an oxidative mechanism of action [27].



The development of this response was dependent on protein synthesis during contact with low concentrations of the substance. Concentrations of up to 1% of hydrogen peroxide, which killed the 'non-adapted' yeast, had no effect on the 'adapted' cells. However, the authors do not report whether this was a genetically stable resistance. Due to its generally limited efficacy and safety concerns regarding vapor generation, hydrogen peroxide is not usually used as a disinfectant on large open surfaces. The importance and even the exact nature of the described 'adaptation' in practice therefore remains unknown [28].

Genuine resistance to formaldehyde has been reported in members of the Enterobacteriaceae and P. aeruginosa. This resistance was plasmid-borne in Enterobacteriaceae and chromosomally determined in P. aeruginosa and genetically stable in each case. Resistant strains were not killed by up to 3000 mg/L formaldehyde, a concentration which is normally regarded as microbicidal. Due to toxicological considerations, aldehydes are used less frequently in open-surface disinfection applications. The frequency of occurrence of resistant strains in healthcare settings has not been investigated. Resistance to triclosan could be triggered in a limited number (five of 40) of bacterial strains of different species by sublethal exposure, but not for the majority of tested strains [22]. The same species occurred in such settings in different parts of the world in the early 1990s, indicating possibly that this was a case of intrinsic rather than acquired resistance of this species. It is perhaps unlikely that this was an adaptive process, but this was not assessed in the report. The same was true for a report describing Bacillus subtilis and Micrococcus luteus isolates from endoscope washers, using chlorine dioxide as a disinfectant. These showed cross-resistance to the oxidative biocides peracetic acid and hydrogen peroxide [29]. Microbial kill was still demonstrated in efficacy tests, but prolonged contact times were needed to pass standard tests. However, chlorine dioxide is extremely sensitive to interference from organic soil leading to lower use-concentrations of this biocide, if an organic burden is introduced into the disinfectant solution. Again, the possibility of such an adaptive process explaining these results was not investigated in this study, but the authors considered such effects in the discussion [30]. Resistance to biocides has other implications, if there is also cross-resistance to antibiotics. The question has been raised, whether the use of biocides selects for antibiotic resistance. Staphylococcus spp. isolated from the food industry P. aeruginosa and Escherichia coli demonstrated cross-resistance to QACs and various antibiotics as a result of their being mediated by nonspecific multidrug efflux pumps encoded by various 'quac' genes which are located frequently on plasmids [31].

These genes can be highly mobile within and between different species. Non-plasmid-borne multidrug pumps have been reported for Listeria monocytogenes. Decreased antibiotic susceptibility was reported for strains selected by subinhibitory biocide exposure. However, the occurrence of such efflux pumps conferring resistance to QACs is not always related to cross-resistance to antibiotics, as has been shown for L. monocytogenes; 10% of 200 isolates showed increased MIC of a QAC and exhibited proton motive force-dependent ethidium bromide efflux, but none of these showed increased MICs to representatives of 15 different antibiotic groups. An inverse correlation between chlorhexidine susceptibility and antibiotic resistance of several clinical isolates has been demonstrated [32]. However, the MBC of chlorhexidine against all these strains was not >130 mg/L, which is well below commonly used concentration of this agent. Exposure for 48 h to sublethal concentrations of chlorhexidine led to increased MICs to cefotaxime, vancomycin, gentamicin, cefuroxime and oxacillin against epidemic methicillin-resistant S. aureus (MRSA)-16, although these workers did not re-examine the isolates

after removal from the chlorhexidine, and the significance of this observation remains unclear. S. aureus isolates with a stable increased MIC of triclosan did not show increased antibiotic resistance. Co-transfer of low level triclosan and high level mupirocin resistance has been described, although transcipients and donor strains with triclosan resistance did not have a slower rate of kill when exposed to triclosan. Other authors report cross-resistance of triclosan-adapted E. coli to chloramphenicol and trimethoprim. A range of different bacterial species with increased triclosan MIC showed no antibiotic resistance. By contrast, triclosan-tolerant E. coli were significantly more susceptible to aminoglycoside antibiotics than other strains. The possible effects of the misuse of biocides at below use concentrations in the medical area have been summarized and discussed by McBain and Gilbert [33]. It is obvious that contact of microbial communities with sublethal concentrations of biocides can select for strains with an increased MIC of antibiotics, although this has been observed at a different frequency, depending on the type of biocide. Many data on microbial resistance are derived from laboratory studies. The relevance of microbial resistance to biocides may also be assessed using efficacy data for disinfectants against healthcare-associated environmental and clinical isolates. antibiotic-resistant bacteria do not necessarily show reduced susceptibility to biocides, although such effects have been reported for clinical isolates at the MIC level and even at the microbicidal level [24]. However, it was not determined whether these were intrinsic or acquired resistances, and isolates are often not typed to see how many different strains are being examined, neither are they screened for biocide-related resistance genes or further examined to explore whether these genes are being expressed.

A clinical isolate of Klebsiella oxytoca showed reduced susceptibility to the aldehyde-based surface disinfectant used in that hospital. After analysis of the situation, the authors concluded that it was probably incorrect handling of cleaning devices that triggered development or selection of the resistant strain [34]. Storage of these devices under soiled, wet conditions may have led to biofilm development facilitating this process. Batra et al. reported recently a significant increase in acquisitions of MRSA, carrying chlorhexidine resistance loci qacA/B upon introduction of a body decontamination regimen using chlorhexidine. The isolated strains showed increased MBCs against this chemical agent, although these still remained well below use concentrations. Interestingly, the outbreak was terminated despite continuing the same disinfection decolonization/suppression regime, so the effect of the laboratory-observed increased MBC on practice remains questionable. Many reports demonstrate the efficacy of disinfectants against clinical isolates, even if used routinely in the corresponding setting [21, 23, 35]. Although most studies show that clinical isolates are susceptible to correctly applied disinfection regimes, the need for further investigations to understand the significance of antimicrobial resistance for the healthcare environment has been pointed out. Other authors conclude that even the broad use of biocides in consumer products has not led to relevant biocide resistance phenomena in practice, based on field studies [18, 29, 32]. surveillance of microbial survival in disinfectant-use solutions in practice and of microbial survival on disinfected surfaces and devices are needed to understand the situation. If the same strains are isolated repeatedly, these will have to be tested for susceptibility to the corresponding biocides.

Conclusions

The threat of antimicrobial resistance (AMR) is growing at an alarming rate and the situation is perhaps aggravated in developing countries due to gross abuse in the use of antimicrobials . It is well known that any use of antimicrobials however appropriate and justified, contributes to the development of resistance, but widespread unnecessary and excessive use makes the situation worse . Misuse of antimicrobials is facilitated in developing countries by their availability over the counter, without prescription and through unregulated supply chains . Non-compliance in the use of antimicrobials has many repercussions upon resistance and poverty is a major root factor of antimicrobial misuse in developing countries . On the other hand, even among the rich, some patients miss doses either by mistake or deliberate, especially in cases where signs and symptoms begin to subside after an initial favorable therapeutic response . In other situations,

such as in the event of an acute side effect, patients abandon their treatment, only to return to the hospital with a recurring infection by a more virulent and resistant strain of the microbe . These actions result in the exposure of surviving pathogens to sub-therapeutic concentrations of antimicrobials thus increasing the chances of acquiring resistance. Self-medication is a common practice in developing countries where patients often get antimicrobials without prescription and through unregulated supply chains . To make the situation even worst, some patients seek their first-line of treatment from traditional healers who provide them with herbal combinations for the treatment of infections. These substances of unknown composition and potency may enhance pathogen fitness and contribute to the development of resistance. Antimicrobial resistance often occur through the inhibition of specific antimicrobial pathways such as cell wall synthesis, nucleic acid synthesis, ribosome function, protein synthesis, folate metabolism, and cell membrane function.

Conflict of interests

The authors declared no conflict of interests.

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