CLINICAL SIGNIFICANCE OF NOSOCOMIAL EMERGENCE OF BACTERIAL ANTIMICROBIAL RESISTANCE: A REVIEW

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ABSTRACT
Hospital acquired infections (HAI) are called nosocomial infections, which comprise a considerable burden on the patients and healthcare delivery worldwide. Antimicrobial resistant organisms pose an increasing threat, although multiple resistant pathogens are still in the minority. Many global networks and initiatives are addressing this threat with variable degrees of success. Antibiotic resistance control has a high profile but the same is not true for biocide resistance. Many issues relating to biocide resistance are examined, the paradigms with antiseptic use are explored and ways in which biocide resistance could threaten the prevention and control of HAIs (nosocomial infections) are described in this review paper. Several proposals to inform the need and nature of surveillance, prevention and control measures are made.

KEYWORDS: Nosocomial infections, hospital, antimicrobial, NWFP, bacteria, pathogens

INTRODUCTION
Antimicrobial resistance is a global issue of great importance; the possibility of untreatable infections is ever high (Cookson 2000a). In response to this, the World Health Organization has advocated a multi-disciplinary Global Strategy in an attempt to address the multidimensional view of the problem (Anonymous 2004). The European Union (EU) also considers the threat of antimicrobial resistance to be extremely serious and has established several interactive surveillance networks and research project.

Nosocomial infection is a serious threat to millions of US inpatients yearly and carries a high rate of mortality (approximately 5%). All hospital clinicians have a role in helping to prevent and appropriately treat nosocomial infections. In particular, certain surgical procedures are among the risk factors for nosocomial infection, especially with multiple resistant pathogens. There is a need to educate and update surgeons regarding procedures to control nosocomial transmission of pathogens and to prevent infection when possible. The appropriate prophylaxis and empiric antimicrobial treatment when infection occurs is of paramount importance in surgical patients in order to minimize the development of resistance, which can increase hospital length of stay and results in higher mortality (Anonymous 2007).

Antimicrobials comprise antibiotics and biocides. Antibiotics may be used for systemic or topical treatment of infections, preventative therapy of contaminated sterile sites, e.g. catheterized urine (Olson and Cookson 2000) and prophylactic use, e.g. for per operative colonic or orthopedics surgery (Song and Glenny 1998; Glenny and Song 1999). Biocides comprise topical agents (antiseptics), disinfectants, sterilants and preservatives.
Although resistance to antibiotics has been addressed in many strategies and publications, the complex issues and importance of biocide resistance has not yet achieved as high profile and this is explored in this review article.

The relationship of nosocomial infections
The hospital environment has a complex ecological context. At a time approximately 10% of patients in hospitals suffer from a hospital acquired infection (HAI), defined as those occurring 48h after a hospital admission (Emmerson 1995). Most HAI pathogens are of a low grade, so colonization always exceeds infection (Anonymous 1995, 1998). Unless one identifies the total reservoir of colonization for many pathogens, control will be difficult, if not impossible (Anonymous 1995, 1998). An important concept in HAI is the interaction between the germs (the microbe), the soil (the patient; hospitalized patients are often more vulnerable to infection) and the climate (the environment, which includes all the equipment that may be in contact with patients, and also comprises more abstract aspects of healthcare delivery, such as the effect of inadequate staffing and bed shortages; Cookson 1997a).

Hospital acquired infections comprise an enormous socioeconomic burden; a recent study in England estimated this to be approx. 1 billion pounds per year (Plowman et al. 2001). These costs included Those incurred during hospital stay, and others incurred after discharge. In under developed countries and low socioeconomic areas of the world, these nosocomial infections are manifolding problematic for society and hospital personals. Awareness level of patients and patient’s attendants is of significant low level and this may cause some time very dangerous situation in case of contagious viral infections. In poor and under developed countries such type of cost/estimated base studies are not conducted, however this HAIIs, would have high impact in this respect. However, although this was one of the most detailed studies conducted so far, the figure was an under-estimate, in the sense that it did not consider infections in high-risk settings such as intensive and neonatal care and specialized units, e.g. for liver, renal and transplantation, where infections may carry a higher morbidity and cost. Neither did it attempt to estimate costs of attributable mortality due to HAIIs, a rather contentious area. Estimates of mortality directly or indirectly due to HAIIs vary, but probably comprise 1–4% of all HAIs in developed countries and 2–9% in underdeveloped countries (Haley et al. 1985; Plowman et al. 2001).

An approximately equal number of patients in hospital suffer from infections acquired in the community (Emmerson 1995). As for patients colonized or infected with HAI pathogens, such patients are a potential source for cross infection to others in hospital. Antimicrobials can be used in the community or the hospital environment; resistance emerging from their use or misuse in either setting will thus have implications in the hospital environment (Gilbert and McBain 2001). This rubric is made all the more complex by the increasing realization that many patients colonized or infected with HAI pathogens will have acquired these during stays in other hospitals, including those abroad or during previous stays in that same hospital (Cookson 2000b; Cooper et al. 2003). Nursing homes are now the second most frequent source of MRSA challenges to English hospitals (Cookson 2000b). These dynamics make the design of surveillance, prevention and control measures for more of a challenge, it being much more difficult now to attribute the isolation of a resistant HAI organism to antibiotic prescribing or infection control activities during the patient’s journey in the admitting hospital.

Thus, new systems are needed that will produce meaningful surveillance data to inform these prevention and control measures (Cookson 1997b). Surveillance data should provide information for action by monitoring the emergence of resistant pathogens and could include, for example, screening of admitted and discharged patients on high-risk units so that acquisitions are identified (Cookson 1997b). This surveillance, control and prevention activities need to be audited and reviewed in interactive surveillance and audit cycles. Surveillance of hospital infection should also be kept on high priority in all countries. There should be national networks in place using harmonized methodologies agreed in a network infection control through surveillance. Up to a third of HAIs are potentially preventable (Haley et al. 1985). The context of biocide resistance in relation to their role in the prevention of HAIs is described below.
Clinical significance of antibiotic resistance

The honeymoon is over. Sequential successive families of antibiotics have been used and abused either with extreme medico ethical cautions or by blind quackery approach. Even in countries with more appropriate prescribing habits, resistance to antimicrobials has emerged and in some instances is increasing (see EARSS website data). In countries where appropriate prescription rules and laws are not followed or bothered by the medical professionals, the speed with which resistance to newly invented antibiotics can be extremely rapid or even precede their use (Cookson and Phillips 1988; Cookson 2000a). A debate has raged for many years as to whether antimicrobial resistant pathogens are less fit than their susceptible parents. The debate needs to be focused on specific microbe-drug combinations and to be underpinned with typing information; recent data would suggest that microbes are able to adapt to the additional genetic load of extra resistance genes (Gillespie 2001). Thus the removal of antimicrobial selection pressure may not result in the emergence of sensitive progeny or their replacement with more susceptible clones.

Many pharmaceutical companies are withdrawing from the market. There has been a disappointing lack of success in discovering new antimicrobials there are, for example, no anti-Gram-negative agents under development that will be available in the next 10 years. Patents do not provide sufficient time to recoup the investment spent on antibiotic development. Companies are thus reluctant to provide additional funds for future antimicrobial development from other more profitable areas of their portfolio. National requirements for lack of toxicity and improved clinical outcomes are also becoming more difficult, or expensive, to satisfy. New high potency antibacterial drug development for pharmaceutical companies is big challenge due to present speedy drug resistance trends. Clinicians are thus faced with very few therapeutic options for several HAI pathogens. However, it must be emphasized that such occurrences are currently for the minority of therapeutic situations (Cookson 2000a). Glycopeptide-resistant enterococci antibiotic therapies were overviewed previously (Cookson 1998a). The various imitations were described; lack of clinical effectiveness, toxicity, bacteriostatic rather than bactericidal activity and the ease of emergence of resistance to new antibiotics. Resistant enterococci are very low-grade pathogens, but were glycopeptide-resistant Staph. aureus to become more widespread and behave as virulently as more sensitive strains, they would pose a considerable therapeutic challenge (Arakawa et al. 2004; Tenover et al. 2004). This situation is also evident in Gram-negative rods with the emergence of extended spectrum b-lactamase and carbapenemase producing organisms (Shannon et al. 1998; Henwood et al. 2002; Poirel et al. 2003). In infections caused by these organisms, only therapeutic agent may be colistin, a potentially nephrotoxic agent.

Issues of biocide resistance

There are many puzzling factors that broke any discussions relating to biocide resistance. Firstly, there is no international consensus on biocide efficacy tests or even an approved product register of products in some countries. Secondly, in some countries there is little or no legislation preventing the sale of ineffective or unsuitable disinfectants. Thirdly, there is no consensus as to the correct tests for determining biocide resistance. Assays that have been used include the minimal inhibitory concentration (MIC), various rates of kill tests, some of which have international agreed status, and in-use tests. Then there are a variety of clinical tests such as the glove juice and the Story ring test (Cookson et al. 1991a). Although many HAIs are caused by microbes in biofilms, most laboratories are not using biofilm methodologies (Stewart and Costerton 2001) to assess biocide (or indeed antibiotic) effectiveness. Reference and perhaps even clinical laboratories need to consider adopting such methods where current methods are not predictive of clinical relevance?

Unlike antibiotic resistance, the issues relating to biocide resistance have a very low profile and priority. This is surely not helped by the various issues outlined above. Earlier some reference laboratories performed testing, but this became a lower priority or such activity was viewed to be more appropriately performed in accredited commercial laboratories. This low priority is also reflected in the lack of funding of biocide research projects in most countries.
When biocide resistance data are presented rarely, if ever, are they a product of a structured surveillance and epidemiological approach? National or international surveillance is not in place and the epidemiological context of resistance seen in a particular clinical setting, and generalizability of such findings are uncertain. It is known from an extensive literature on antibiotic resistance that, depending on the drug and bacterium, it can vary geographically and over time (Cookson and Phillips 1988; Anonymous 1998; see also the EARSS website). There is no reason why biocide resistance should be any different. Another deficiency is that, studies often fail to identify the biocide resistance mechanism, its genetic nature or location. This is no doubt related to the lack of investment outlined above. Such mechanistic and genetic location data could provide important insight into current or possible new problems and their trends, the use of general (e.g. efflux and impermeability) or specific resistance mechanisms, their carriage on transposons, integrons or plasmids and the inclusion in these of antibiotic resistance genes. These data would provide potential insight to the relevance of the selection pressure to various HAI pathogens. They are also pivotal in understanding the important area of cross-resistance between biocides and antibiotics and the potential for biocide use to increase antibiotic resistance. This has been widely discussed and the consensus is that biocide use is of much less importance than antibiotic use in the emergence of antibiotic resistance (International Scientific Forum on Home Hygiene 2000; http://www.ifh-homehygiene.org/2003/2public/antresFINAL.pdf; April 2005; Gilbert and McBain 2001). However, there are many gaps in our knowledge because of all the deficiencies alluded to above. It will not be possible to describe the current situation, monitor trends or inform prevention and control measures unless there is more attention paid and resources devoted to explore the issues further.

HAI: Type, prevention and possible implications of biocide resistance
Hospital acquired infection can be classified in number of ways, for example by the site of the infections or microbes implicated. A useful, even though over-simplified, approach is one of causation and prevention, and this approach is used to consider the possible implications of biocide resistance. HAIs comprise autoinfection, cross-infection and infection from the environment.

Auto-infection
Auto-infections are caused by organisms carried by the patient upon admission to hospital and usually comprise the majority of HAIs (Haley et al. 1985). Prevention is by protecting the portal of entry to the microbes. This can be controlled by using careful aseptic technique during operations, the insertion of sterile devices, for example, into blood vessels, the trachea or bladder. Antiseptics are also applied to the skin or mucous membranes prior to such interventions. Resistance to such biocides would result in a higher infection rate, which would probably differ between operation types, operators and result in the use of prophylactic antibiotics in clean, non implant, non critical surgery where it is currently not indicated. Resistance would thus increase prophylactic or topical antibiotic prescribing selective pressure with the increased likelihood of the emergence of resistance to the antibiotics used in this way, many of which would also be used to treat infections. Thus biocide resistance has the potential for a serious knock-on effect on resistance (or indeed cross resistance) to valuable antibiotics increasing the possibility of untreatable infections.

The use of urinary and central venous catheters increases the likelihood of an HAI approximately sevenfold (Glynn et al. 1997). We must thus try to reduce the frequency and duration of their use; this will include the use of alternative methods of drug delivery. An alternative strategy to reduce these HAIs has been to design catheters with various incorporated biocides and antibiotics (Tambe et al. 2001). Many infection control teams are concerned about the indiscriminate use of these antimicrobial impregnated devices. Will they result in the incorporated biocides or antibiotics producing antimicrobial resistance selective pressure? If resistances were to emerge, such devices would no longer be effective, further stressing units with device related infection problems, and perhaps increasing the problems of resistance to therapeutically useful antibiotics as described above. Their use should not be a replacement for avoidance of device usage and continuous quality improvement programmes of correct usage (Mermel et al. 2001).
Many units are using these devices, and it will be particularly important to monitor trends in the relevant biocide resistance to provide infection control teams and clinicians with the information needed for their risk assessments. Monitoring the resistant isolates to related cross-resistance to other antimicrobials would also need to be considered.

**Cross-infection from other patients or staff**
Cross-infection with HAI microbes can occur from the hands of staff during surgical or device insertion related procedures. They more often are transferred on the hands of staff following close contact patient procedures. The evidence for the reduction of colonization and infection with HAI organisms has been well reviewed: hand hygiene is the most important and effective measure to reduce such occurrences (Teare et al. 2001). Biocides are thus important, in that they reduce the likelihood of infection when incorporated into soaps or gels. Disinfectant-containing soaps are used to reduce the total hand microbial flora in surgical disinfectant scrubs. They are also effective in removing transient microbial flora acquired following close contact patient procedures. Alcohol gels are now the new hand hygiene standard to be used on unsoiled hands (Teare et al. 2001). Disinfectant containing soaps are also advocated in outbreak settings or on high-risk wards/units such as intensive care. Resistance to biocides used for hand hygiene would also have severe implications for increased HAIs due to cross infection. If there were cross-resistance or co-transfer of resistance, to antibiotics the implications would be even more ominous, as described above. Antimicrobial impregnated devices will also have a protective effect against cross infection. However, this is not the ideal way of preventing such occurrences and could be discouraged, in theory of hand hygiene compliance (Stanton and Glendon 1996). Another strategy that can be used to decrease cross infection is to reduce the HAI organism reservoir. Examples of this include the use of antiseptics and biocides to clear antibiotic-resistant organisms, e.g. MRSA in colonized patients and staff (Anonymous 1998). We discuss below the paradigm relating to disinfectants used in this way. At this juncture, suffice it to say that the implications are increased cross infection and the possible use of antibiotics to decolonize patients, with the increased risks of antibiotic resistance alluded to above. In fact the emergence of resistance to mupirocin is a good example of the implications of this scenario (Cookson 1998b). Fortunately, there is no cross-resistance between this agent and other antibiotics, although resistance to other antimicrobials can co-transfer with mupirocin resistance (Cookson 1998b). It is important to point out that biocides can on occasion also be used as topical agents to treat infected sites in patients, e.g. pressure sores infected with MRSA. Such use can avoid the need for antibiotics and, when used with systemic antibiotics, will reduce the microbial biomass and potential for the development of antibiotic resistance. This strategy has been one of the drivers to produce new topical antimicrobials (Embleton et al. 2002).

**HAI from the environment**
The environment has an enormous potential to cause HAIs. The preventative strategy is to reduce the reservoir for potential infection where there is a significant risk of infection, i.e. where the reservoir could become the source of HAIs. The major sources are items of equipment used directly on patients after use on other patients, contact with staff hands or contamination in the environment, e.g. by dust, nonsterile water, insects. Many of these have been resolved with effective hospital sterilizing and decontamination services with quality systems, clearly written, agreed and taught policies, procedures and audit cycles in place (Anonymous 1998). The decontamination of heat sensitive equipment would be threatened by the emergence of significant resistance to the chemical sterilants used in these procedures. The emergence of resistant mycobacteria is a cause for concern, which needs to be monitored (Stanley 1998). The use of biocides as preservatives is a more specialized area, but one where resistance would have major implications for HAIs. The implications are evident now where such preservatives are misused (Cookson et al. 1988). Decontamination of the general ward environment is a more contentious issue. For certain HAIs, there is some evidence for an environmental role in HAIs. These include Gram-negative rods, enterococci and Clostridium difficile (Cooke et al. 1994; Anonymous 1995; Dancer 2004), although much of the evidence remains contentious (Hosein et al. 2002), even more so for MRSA (Anonymous 1998).
Recently, 40 infection control scientists from 18 countries reported that there are insufficient data to justify recommendations of routine surface disinfection in hospitals other than that of high-risk areas (e.g. isolation units) or possibly to prevent transmission of high-risk organisms (e.g. MRSA) (Allerberger et al. 2002). They point to the possible side-effects of biocides to patients and healthcare workers and the risks to the environment of non-biodegradable compounds and others that release carcinogens. Proposed standards have been made recently (Dancer 2004). They will need a more scientific evidence base before they can be implemented.

The Paradigm of Biocide Resistance: An Illustration
The scenario of the use of antiseptics and biocides to decolonize patients carrying MRSA serves as a good example to explore many of the issues raised above. There is a good evidence base for the use of mupirocin to decolonize patients and reduce the reservoir for possible auto-infection and cross-infection to other patients (Anonymous 1998). Mupirocin resistance has been described as a cause of failure in MRSA control (Cookson 1998b), and a recent survey of infection control teams found on univariate analysis that it was a significant factor (0% compared with 14/E7%; P < 0/E05) in failure to control MRSA outbreaks (Cookson et al. 1998). Resistance has been related to prolonged and prophylactic use of the agent (Cookson 1998b). When the first epidemic MRSA (EMRSA-1) caused outbreaks in the UK, we were aware that it could carry a quaternary ammonium resistance gene (qacA) on a gentamicin resistance plasmid that encoded for an efflux mechanism resulting in low-level chlorhexidine (CHX) resistance (an elevated MIC). We established that these isolates were not killed more slowly in an *in vitro* rate of kill test. Methicillin sensitive Staph., aureus (MSSA) transipients with the qacA gene transferred to them from EMRSA-1 were also killed rapidly *in vitro* and *in vivo* (Cookson et al. 1991a). Interestingly, the plasmid could be readily lost during these tests and needed to be checked that it was still present in the strains postexposure to ensure that the effects of the qacA were indeed being explored. This had not been done previously by other workers and may have explained the previous discrepancies found in the literature (Cookson et al. 1991a). CHX MICs of EMRSA-1 isolates with different pulsed field gel electrophoresis genotypes from six geographically disparate hospitals were not further elevated 6 years after the first appearance of the strain (B. Cookson, unpublished data). The plasmid was not incorporated into the chromosome in these strains as described previously (Rahman et al. 1988). Additional unpublished data would suggest that the qacA CHX resistance gene did not convey a significant advantage to EMRSAs, in that resistance to gentamicin and CHX of the isolates referred to the reference laboratory fell from c. 90% in 1984 to c. 50% in the late 1980s.

This apparent lack of significant low-level resistance may be contrasted by the situation for triclosan. We made the first description of transferable triclosan resistance in MRSA in 1991 (Cookson et al. 1991b). The investigation was initiated by a hospital that had been using the agent intensively for about a year. High-level mupirocin resistance had been observed locally and then the strains would not clear with triclosan from sites that included the axilla and groins. Switching to chlorhexidine decontamination cleared the MRSA from colonized sites (R.P.J. Garvey and M.R. Price, personal communication). We examined the isolates and found that the high-level mupirocin resistance and low level triclosan resistance (MIC 2–4 mg/l) transferred and cured together. When MSSA transipients and MRSA donors were examined, they contained a curious plasmid that co-migrated with the chromosome. Similar plasmids had been seen in the original mupirocin-resistance strains (Rahman et al. 1989). There was no resistance to other biocides and two extra EcoR1 bands were seen when the triclosan/mupirocin resistant plasmid enriched chromosomal bands were examined compared with those which were solely mupirocin resistant. Interestingly, the rate of kill of various strains was always in the same peck order when tested together (Fig. 1). Representatives of all the MRSA that were referred to the reference laboratory in 1992 were examined and no other isolates with low-level triclosan resistance were found. We could not train the triclosan-resistant strains to higher triclosan MICs, although MSSA and EMRSA-1 could be trained to similar low-level triclosan resistance (MIC 2–4 mg/l). Interestingly the resistance in these trained strains was stable when the strains were left for 2 years on agar slopes.
A triclosan susceptible MRSA strain consistently had poorest rate of kill in our tests (Fig. 1). It was always sensitive to triclosan when survivors from the test were examined by MIC testing. The same phenomenon had been observed previously, in that a CHX MIC-sensitive strain (an MSSA) had the poorest rate of kill to the biguanide and survivors were always sensitive to CHX (Cookson et al. 1991a). Perhaps there are biocide resistance mechanisms of which we are unaware, that are not detected by an MIC test? Interestingly isogenic MRSA with and without plasmids and mupirocin and triclosan resistance had identical rates of kill (K247 and K247c in Fig. 1). These results raise very interesting questions about the significance of raised MICs to biocides that are bacteriostatic at low concentrations and bactericidal at higher concentrations (Russell 2004). All these interesting isolates should be examined in biofilm systems. As mentioned previously, these questions may be more relevant to HAIs, and to survival in the hospital and community environments, where lower biocide levels may be relevant (Stewart and Costerton 2001). Unlike the situation with CHX, there have now been other reports of higher-level triclosan resistance in Japan (50 mg l\(^{-1}\); Sasatsu 1993) and in the UK (32 mg l\(^{-1}\); Bamber and Neal 1999). In neither instance was the clinical background or significance described. Others have reported no triclosan resistance increase in UK EMRSA-15 and 16, although they did find 10 other MRSA isolates, including representatives from two other EMRSAs, with MICs of between 1 and 4 mg l\(^{-1}\) (Al Doori et al. 2003). However, in agreement with Bamber and Neal (1999) increases in triclosan MICs should be considered and more should be done to explore their significance and occurrence than at present. For example, periodic surveillance of referred isolates to the Reference Laboratory and/or design of sentinel surveillance schemes underpinned with local infection control review of topical disinfectant effectiveness should be introduced.

**Prevention and Control of Antimicrobial Resistance**

Clinical governance emphasizes the importance of evidence based practice (Hosein et al. 2002). As mentioned above, it is clear that the evidence base relating to biocide resistance needs to be improved. This includes agreement on measuring and interpreting the results of microbial biocide resistance. Well designed and reviewed surveillance systems are required, which should include the epidemiological context needed to inform the nature of the selection pressure for the observed resistance. Such information would include biocide types and quantity used per patient and, how and when they are used. These systems need to be reviewed regularly to ensure adequate geographical coverage and appropriate denominators. It is essential that the surveillance be combined with microbial typing information and identification of the resistance mechanisms and their genetic location. Reference and research laboratories should be funded to perform additional studies to underpin this work as outlined above. They should also develop appropriate and user-friendly resistance detection systems for clinical laboratories were a resistance to emerge that was of great clinical importance. Interestingly, typing laboratories abandoned resistotyping many years ago because of problems with typability, reproducibility and discrimination. Some of these systems included biocides; they should perhaps be revisited and the role of molecular biology, including the use of microarrays, reconsidered.

Reference and research laboratories should evaluate biocide resistance in any important new or multiple antibiotic-resistant organisms, e.g. linezolid or glycopeptide-resistant enterococci and staphylococci, carbapenem resistant Gram-negative rods. Laboratory simulations could also include the ability of antimicrobial agents to increase or decrease the rate of transfer of biocide (Pearce et al. 1999) and antibiotic resistance to assist in the prioritization of control measures and the design of strategies such as rotating the use of biocides (Murtough et al. 2000) and antibiotics (Raymond et al. 2001). Epidemiological studies will also be needed to establish the validity of such interventions and provide additional information to inform practice. All planned intervention studies should comply as much as feasible with recent study design recommendations (see Appendix 5 in Cooper et al. 2003). Many studies of antibiotic resistance have emphasized that we need two prevention and control approaches. These comprise improved antibiotic prescribing practices to reduce the likelihood of the development or selection of resistant organisms and improved compliance with infection control practices to reduce the spread of these resistant organisms (Hosein et al. 2002). There also needs to be induction, and ongoing, education and training of healthcare workers in these practices.
These prevention and control systems need to be validated with interactive surveillance and policy/practice audit cycles to improve these practices. Many studies have shown that, for interventions such as these, where there is a complex contextual background, sustained improvement in prevention and control measures needs ownership of the interventions by healthcare workers, some sort of feedback to them of surveillance and/or audit data and opinion leaders amongst them who believe in, advocate and are seen to be complying with, the proposed interventions (Naikoba and Hayward 2001; Redfern et al. 2003). This approach is interactive with, and directly transportable to the prevention and control of biocide resistance. This requires healthcare workers to be trained to comply with clear and agreed policies and practices. The main difference will be the strategies to improve biocide use locally. They need to avoid unnecessary and incorrect use of biocides. Decontamination methods will depend on the risk assessment of the use of equipment (Rutala and Weber 1999), which should be cleaned before decontamination to avoid biocide inactivation by organic matter. Heat rather than biocides should be used wherever possible (it is cheaper, more controllable and of consistent effectiveness). There should be good housekeeping, including the use of the correct biocides before their expiry date and at the correct concentration. Staff should use procedures that avoid leaving biocide residues, which may increase the selection of resistant strains (Rutala and Weber 1999).

This review article has attempted to outline the many deficiencies in knowledge regarding biocide resistance and its clinical impact. It is essential that endeavors continue to understand how bacteria respond to antimicrobial pressures in various ecological niches and the reasons why lower as well as higher resistance levels are encountered. This knowledge has to inform and be informed by international surveillance programmes on the occurrence of biocide resistance, the emergence of new resistances and trends over time. Only in this way can it be ensured that appropriate interventions are designed, implemented and monitored.
REFERENCES


