ANTI-BACTERIAL SKIN DISINFECTANTS IN THE REDUCTION OF METHICILLIN RESISTANT *STAPHYLOCOCCUS AUREUS* (MRSA) SKIN COLONISATION

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SUMMARY

In health care establishments there has been an emergence of multiply resistant organisms such as methicillin resistant *staphylococcus aureus* (MRSA). This has highlighted the need to re-evaluate not only, medical, nursing and infection control practices, but the methods of management and treatment in an attempt to reduce/eradicate the spread of the organism from patients and therefore minimise the risks of cross infection.

As part of the routine care and management of patients with MRSA, antibacterial agents are widely used as body washes to reduce/eradicate skin colonisation of the organism. The aim of this research was to investigate the effectiveness of washing with chlorhexidine, triclosan or a soap solution for eradication of MRSA from patients following one course of body washes.

Whilst the overall numbers were too small to reach statistical significance, this research project has served to demonstrate that in the clinical environment there is little difference between triclosan, chorhexidine or soap. Minimum inhibitory concentration (MIC) testing demonstrated that triclosan was more active than chlorhexidine against MRSA, which in turn was better than soap. This would suggest that when selecting a body-wash the effectiveness of the agent used is influenced by its application. From a review of the literature and the evidence presented in this study the use of topical mupirocin to eradicate nasal carriage of MRSA was shown to have had little effect. Given the potential for antibiotic resistance, consideration should be given to the routine use of mupirocin for nasal carriage of MRSA. Therefore, infection control programmes aimed at reducing MRSA skin colonisation should consider both the residual effects of antibacterials in relation to the patient's length of stay, giving consideration to the use of antibacterials for 'short stay' patients and the patient's clinical condition and the environment in which they are nursed.

Key words. chlorhexidine, triclosan, MRSA, skin disinfection

DEDICATION

This work is dedicated to my

mother (1920 –1996)

and father with love and respect.

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1. INTRODUCTION

In health care establishments there has been an emergence of multiply resistant organisms, such as methicillin resistant *Staphylococcus aureus* (MRSA). This has highlighted the need to re-evaluate not only medical, nursing and infection control practices, but the methods of management and treatment in an attempt to reduce/eradicate the spread of the organism from patients and therefore minimise the risks of cross infection.

In today's economic climate Hospital Trusts are increasingly called upon both to justify and limit expenditure. Hospital acquired infection not only affects patient's by increasing their length of stay, causing pain and discomfort and necessitating further treatment (Taylor 1986; Caddow 1994) but also increases costs. The additional time and resources required to manage and treat the patient increase already compromised budgets and have a cascading effect on Hospital Trusts as a whole if contractual agreements cannot be met due to bed blockages (Ayliffe *et al.*, 1990; Ayliffe *et al.*, 1992).

The introduction of the Patient's Charter in 1992 (Department of Health, 1993) and more recently, Government initiatives aimed at keeping the public informed have served to heighten patient's awareness and expectations. With this increased awareness some patients acquiring

infection whilst in hospital have chosen to take their concerns through the legal system and seek financial recompense from Trusts if negligence is proven. This has led Trusts to divert funds from direct patient care into indemnity insurance to cover potential litigation suits.

Since the issues relating to MRSA are diverse, this work concentrates on one aspect of the care and management of patients found to be colonised with MRSA. Specifically the project was designed to look at the effectiveness of antibacterial agents used to wash patients positive for MRSA in an attempt to identify the most effective topical treatment available for use and attempt to reduce the risk of cross infection and hospital acquired infections with this organism.

1.1. *Staphylococcus aureus*

Staphylococci are Gram-positive cocci which form grape like clusters, and are classified as non-motile, non spore-forming, aerobic and facultative anaerobes, of which there are 27 different species (Arbuthrott, 1992). Staphylococci can be classified into groups of 'Coagulase negative' and 'Coagulase positive' species, dependent of whether they produce the enzyme coagulase, which clots plasma (Wilson, 1995). Staphylococci differ in pathogenicity, with *S.aureus* being one of the most pathogenic and being responsible for a large percentage of staphylococcal infections (Jones, 1996).

The pathogenic nature of *S.aureus* is dependent upon its ability to produce toxins and enzymes. It can be characterised by two main properties; its ability to produce protein A and coagulase or clotting factor. Protein A is thought to aid adherence and possess anti-phagocytic properties. Coagulase reacts in a similar manner to the activation of thrombin, whereby fibrin is deposited on the surface of the bacteria which may prevent phagocytosis. *Staph. aureus* has the ability to produce other toxins including alpha and beta toxins which are capable of lysing erythrocytes, platelets and damaging smooth muscle (Stanford, 1992; Baron *et al.*, 1994; Brooks *et al.*, 1995).

S.aureus can be transiently carried on the hands, survives well on the skin of healthy individuals and is present in the normal flora of approximately 20%-30% of the general population (Greenwood, 1992; Thomlinson, 1994). Although carried as normal flora by a percentage of the population it is a pathogenic organism and has the ability to cause infection if it reaches susceptible sites in sufficient numbers to initiate an associated host response (e.g. the organism in the nose reaching a break in the skin or a surgical wound causing inflammatory damage to tissues or produce pus,(Mayhall, 1993; Jones, 1996). It is frequently responsible for boils and cellulitis in chronic skin lesions such as pressure sores and venous leg ulcers (Gilchrist and Reed, 1987). If present on a patient's

skin *S.aureus* could be considered a potential risk for both debilitated patients and to other patients as a source of cross infection (Doebbeling, 1993).

Transmission of organisms is well documented by authors such as Greenwood (1992) and Thomlinson (1994) who identify specific routes of transmission as contact, airborne, faecal/oral and blood to blood. *S.aureus* can be isolated from the environment (Cookson and Phillip 1990). Ayliffe *et al.* (1990) discussed the role that the environment plays in the spread of infection and offered advice on the cleaning, disinfection and sterilisation methods to prevent transmission of organisms. Later studies by Ayliffe *et al.* (1992) and Caddow, (1994) go further to define both the practices and precautions which are required to block the modes of transmission and prevent cross infection by the correct use of protective clothing, improved handwashing techniques and isolation of patients.

1.2. Methicillin Resistance

The discovery of the clinical use of antibiotics in the 1940's was seen as a revolutionary move in the care and management of patients with infections. However, it was not long before resistance to antibiotics emerged with the majority of staphylococcal strains initially sensitive to penicillin becoming resistant (Greenwood, 1995). Within four years 65-

85% of hospital staphylococcal isolates were resistant to penicillin, today, more than 90% of strains are resistant (Brook *et al.*, 1995; Greenwood, 1995).

Methicillin is a semi-synthetic β-lactam introduced in the 1960's to combat penicillin resistance. To be active, β-lactams must enter the cell, resist β-lactamase and have an affinity for the essential penicillin binding proteins (PBP's) which are located on the outer side of the cytoplasmic membranes.

β-lactams inhibit the synthesis of peptidoglycan, a major polymer of the cell wall. Peptidoglycan is responsible for maintaining the cell's shape and acts as a buffer against osmotic forces by forming a net-like structure made up of sugar chains cross-linked by peptides. Unlike Gram-negative bacteria, where peptidoglycan forms a thin layer (Nikaido, 1994) or gel (Hobot *et al.*, 1984) between the outer and cytoplasmic membranes, in Gram-positive bacteria the peptidoglycan forms a characteristic thick layer external to the cytoplasmic membrane (Livermore and Williams, 1996).

Staphylococci have four PBPs (identified as 1,2,3,4) of which two (2 and 3) are classed as essential. MRSA have an additional PBP known as 2' or 2a, a unique modified PBP which has a low affinity for β-lactams and is

encoded by the *mec*A gene (Hartman and Tomasz 1984). β-lactams inhibit the final stages of peptidoglycan biosynthesis by binding to this inhibiting the PBPs (transglycosylase/ transpeptidases) responsible for its construction. β-lactams inhibit D-alanyl - D - alanine transpeptidases by acylating the serine group at the active site of the enzyme.

With respect to MRSA, PBP 2' (2a) transglycosylase/transpeptidase has low affinity for β-lactams and continues to function when PBPs1,2,3 and 4 are inactivated. A stable peptidoglycan is produced which has fewer cross-links. At present there are no clinically available β-lactams to significantly inhibit PBP2'. Therefore it can be argued that in the current climate all β-lactams are resistant to staphylococci if PBP2' is present, regardless of individual susceptibility patterns (Hartman and Tomasz, 1984).

Methicillin has been demonstrated to have both a wide range of bacteriostatic and bacteriocidal action against a wide range of Gram-positive cocci such as *S.aureus*. Methicillin resistant strains of *S.aureus* were first reported in 1961 (Jevons, 1961) and since then have been responsible for outbreaks of infection world wide (Keane and Cafferkey, 1984; Casewell, 1986). Today, MRSA is recognised as a significant nosocomial pathogen (Mulligan *et al.*, 1991; Marples and Reith, 1992; Farrington *et a*l., 1990).

1.3. Antibiotic Susceptibility Testing

Several methods have been developed to determine the ability of organisms to develop antibiotic resistance. Within most laboratories once an organism has been isolated it is tested against a series of selected antibiotics to determine its antibiogram. McKane and Kendal (1996) claim that because pathogens have the ability to react similarly to related antibiotics an antibiogram can predict the susceptibility to a range of antibiotics in the same group, therefore avoiding the need for laboratories to test against more than one antibiotic in each group. However, McKane and Kendal (1996) also state that because aminoglycosides do not display cross-resistance there is a need to test this group on an individual basis. A common method used in many laboratories is the disk diffusion method whereby up to 12 selected antibiotic disks can be applied to one plate to determine susceptibility.

An alternative method of susceptibility testing is to determine the minimum inhibitory concentration (MIC). MIC measurement enables a quantitative result to be obtained by measuring the minimum concentration of a specified agent required to prevent multiplication of a pathogen. This ensures that the most appropriate measure and duration of treatment can be administered to optimise the treatment for the patient (Myint *et al.*, 1999; McKane and Kendal, 1996).

1.4. Typing methods

For epidemiological purposes, laboratories use several methods to identify specific bacterial strains. Bacteriophage (phage) typing is one effective method of identifying specific strains of staphylococci. Phage typing exploits the ability of bacteriophages to infect and lyse specific strains of bacterial cells. Phage typing is often used in combination with other methods such as antibiograms as an epidemiological tool to distinguish outbreak strains. However, because of time restrictions placed upon laboratories to produce clinical results, phage typing is not routinely used and is usually undertaken in specialised reference laboratories (Goering RV. 1993).

A more recently developed technique of distinguishing stains of bacteria is pulsed field gel electrophoresis (PFGE). This technique analyses the pattern of fragments of chromosomal DNA produced by selected restriction endonucleases (Goering R.V. 1993). The large DNA fragments produced by the restriction endonuclease are separated by electrophoresis in an agarose gel using a pulsed electrical field. PFGE differs from conventional electrophoresis in a variety of ways. Conventional electrophoresis is based on the fact that negatively charged DNA fragments migrate from the cathode to the anode. With PFGE, electrical pulses of different duration are used. The pulses are applied in varying alignment causing DNA to stop at regular intervals and re-

orientate to a new course (Weller, 2000). The speed of orientation is dependent upon the fragment size resulting in large fragments preferring longer pulse times. These two parameters permit the separation of large fragments of DNA. Because there are relatively few bands of DNA generated by the chosen restriction enzyme, PFGE has proved to be a useful method of discriminating types which is relatively easy to interpret (Mulligan and Arbeit 1991; Linhardt *et al.*, 1992; Layton *et al.*, 1995; Weller, 2000).

PFGE is regarded by many as a proficient epidemiological tool for typing strains of MRSA (Georing, 1993). The use of PFGE is supported in a study by Bannerman et al.(1995) which compared the effectiveness of PFGE as a replacement for bacteriophage typing of *S.aureus* and found the PFGE was more discriminating than bacteriophage typing being able to identify sub groups within each phage group, to type all isolates and distinguish related from unrelated strains of *S.aureus*.

PFGE has been widely used as an established method of identifying strains of *Staphylococci* and in particular MRSA for both epidemiological purposes and in the investigation of outbreaks (Prevost et al 1991; Zaidi et al 1996; Belkum et al 1995; Kluytmans et al 1998). However, whilst PFGE is accepted as a successful method of typing (Bannerman, 1995), it is unlikely to be utilised to its full potential as the preferred technique for

routine clinical use, as the procedure is both time consuming and expensive compared to other methods (Weller T. 2000).

1.5. Disinfectants and antiseptics used to control the spread of MRSA

1.5.1. Triclosan

Triclosan has been successfully adapted for use in the health care setting for more than 30 years as a skin preparation, surgical scrub, oral preparation and in cosmetics. Triclosan is classified as a bis-phenol composed of two phenolic groups (figure 1) which are hydroxy-halogenated.

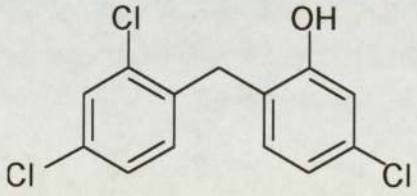


Figure 1 - The structure of Triclosan

Triclosan is a non-ionic, odourless powder, referred to by its chemical name as 2,4,4-trichloro-2-hydroxydiphenyl ether. Several studies have been undertaken to assess its efficacy and safety, demonstrating that it is

a product which is user-friendly, non-toxic and non-irritant (De Salva *et al.*, 1989; Ciba-Geigy Corporation, 1995; Bhargava and Leonard, 1996).

Whilst the use of triclosan has been widely accepted in health care settings, its specific mode of action is under debate. Work by Meincke *et al.* (1980) demonstrated that triclosan diffuses into the bacterial cell, disrupts the cytoplasmic membrane and inhibits RNA, lipid and protein synthesis. Their results on strains of *Pseudomas aeruginosa* indicated that the lipid content of the cell wall could affect the absorption and resistance to triclosan. Studies by McMurray *et al.* (1998, 1999) on the effects of triclosan on *Escherichia coli* and *Mycobacterium smegmatis* demonstrated its ability to interfere with a specific stage in fatty acid synthesis. In *E. coli* the target emzyme is and enoyl reductase, FabI. Genetic evidence suggests that a related emzyme, InhA is the target in *M. smegmatis*. However, McDonnell and Russell (1999) consider that, whilst the specific mode of action is unknown, triclosan has an effect on the cytoplasmic membrane, and support the view that triclosan exhibits specific activity against Gram-positive bacteria.

Since the early seventies several studies have been undertaken to review the antimicrobial effects of triclosan. Vischer and Regos in (1974) demonstrated that triclosan was more potent than either hexachlorophene or neomycin against *S.aureus*. All *S.aureus* strains tested were inhibited

by concentrations of 0.005-0.02 μg/ml triclosan compared to 0.4-1.6 μg/ml hexachlorophene (Vischer and Regos 1974). Equally, later work by Bamber and Neal (1999) to determine the MIC for triclosan against 186 isolates of MRSA and methicillin sensitive *S.aureus* (MSSA) found that there was no significant difference between the incidence of triclosan resistance for MRSA and MSSA. Of the isolates tested, fourteen had MIC $\geq$ 1ppm ($\geq$1 μg/ml) and five had MIC $\geq$ 4ppm ($\geq$4 μg/ml).

Triclosan's versitility, and its ability to exert broad-spectrum activity is well recognised (Ciba-Geigy Corporation, 1995; Bhargava and Leonard, 1996). Its ability to exhibit persistent and cumulative activity against both resident and transient micro-organisms has led it to be widely used throughout health care establishments in the care and management of patients with MRSA as a skin wash (Bhargava and Leoanard 1996; Ciba-Geigy Corporation, 1995; McDonnell and Russell, 1999). However, whilst the use of triclosan has been widely accepted in health care settings, laboratory-based studies have been undertaken which have demonstrated low level resistance to triclosan (Sasatzu *et al.*1993; McMurry *et al.* 1998; Suller and Rusell, 2000). These findings are supported in a study by Bamber and Neal (1999) who recognise that the increased use of triclosan can promote resistance, highlighting concerns as to the potential to encourage resistance when it is used in non health care settings where little control can be given to its use.

Equally, work by Suller and Russell (2000) looking at the susceptibility of *S.aureus* clinical isolates against both triclosan and a range of antibiotics, recognised that while strains of *S.aureus* demonstrate a level of resistance to triclosan, their MIC values do not correlate to bactericidal activity because biocides have multiple target sites. Suller and Russell (2000) also point out that 'pure compounds' should be used in susceptibility testing to prevent other agents such as surfactants and chelators influencing the bactericidal activity of triclosan as the efficacy of antimicrobial products is dependant upon the formulation used.

Other studies undertaken examining the effectiveness of triclosan have focused on its use and application. Bamber and Neal (1999) showed that both the concentration and volume used can influence the clearance rate of MRSA. With studies by Jones *et al.* (2000) suggested that the efficacy of a product may be affected by factors such as the ionic nature of the formulation, type of surfactant used, emollients, detergent base and pH.

1.5.2. Chlorhexidine

Chlorhexidine is a cationic bisbiguanide (figure 2) was first synthesised in 1950 as part of research into sythetic antimalarial agents. It was observed to demonstrate high levels of antibacterial action with low levels of toxicity, whilst having the ability to bind to skin and mucous membranes

leading to its development as a skin disinfectant and preservative (Denton, 1991).

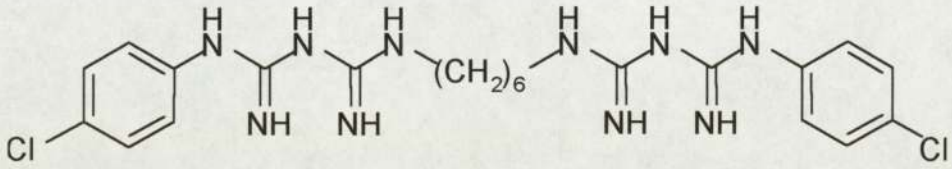


Figure 2 - The structure of chlorhexidine

Chlorhexidine occurs as a whitish crystalline powder and is used in many pharmaceutical agents alone or with other antimicrobial agents such as alcohol or cetrimide. It exerts a broad spectrum of activity on both Gram-negative and Gram-positive bacteria and has been widely adopted for use throughout health care organisations as a hand disinfectant and a skin and oral preparation as well as a preservative and disinfectant. (Russell *et al.*, 1992; McDonnell and Russell, 1999). As a skin disinfectant chlorhexidine is used as a 0.5% solution of the acetate or gluconate salt in 70% alcohol or as a 2% or 4% detergent solution of the gluconate salt (Therapeutic Drugs, 1998).

Several studies have been undertaken to assess both the safety and efficacy of chlorhexidine. Russell *et al.* (1992) found that the activity of chlorhexidine is reduced in the presence of serum, pus, blood or other organic matter. The authors also suggests that, because of the cationic nature of chlorhexidine, its activity is reduced in the presence of soaps and other anionic compounds. This is supported in later work by Russell and Day (1993), which demonstrated that the activity of chlorhexidine is largely dependent upon the pH and the presence of organic matter. The effects of chlorhexidine as a single agent or in conjunction with other agents have been widely studied for both efficacy and safety. An early study by Lowbury and Lilley (1973) assessing the effects of chlorhexidine in conjunction with other agents found that chlorhexidine in an alcoholic solution was an effective skin disinfectant. However, a later study by Rutter, (1983) demonstrated cases of haemorrhagic skin necrosis associated with umbilical artery catheterisation in extreme pre-term infants that were attributed to the use of alcohol from a solution of chlorhexidine 0.5% in a 70% spirit as a disinfectant. Other studies reviewing the safety of chlorhexidine have highlighted cases of hypersensitivity and anaphylactic shock (Cheung and O'Leary, 1985; Evans, 1992; Chisholm, 1997).

1.5.3. Other antibacterial agents

When considering the effectiveness of body washes as a means of reducing MRSA carriage, the composition of agents designed to be 'gentle washes' or 'non medicated' needs to be considered to ascertain if any additives have antibacterial activity. As part of the research currently being undertaken, it was identified that one the three agents used was soap, which contained 2-bromo-2-nitropropane-1, 3-diol (bronopol), an antibacterial agent commonly used as a preservative in soaps and shampoos.

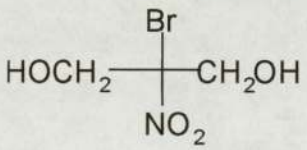


Figure 3 - The strucuture of bronopol

Bronopol (figure 3) is a white, or almost white, odourless crystalline powder. Bronopol is freely soluble in both water and alcohol. The stability of bronopol can be affected by heat and an increased pH above 8. As an antibacterial agent bronopol exerts a broad spectrum of activity,

particularly on *Pseudomonas aeruginosa*, but is considered less active on yeasts and moulds (Scott and Gorman, 1998; Therapeutic Drugs, 1999).

1.6. Studies undertaken reviewing the effectiveness of chlorhexidine and triclosan as antibacterial agents.

Numerous studies have been undertaken to assess the efficacy of skin disinfectants containing chlorhexidine gluconate or triclosan. Many of these have compared the activity with that of povidone-iodine to reduce skin flora on the hands of healthy volunteers as opposed to clinical trials on patients found to be colonised with multi resistant organisms such as MRSA. Of those studies undertaken assessing the ability of antibacterial agents to either remove or eradicate organisms the majority have been conducted within a controlled environment as opposed to clinical settings. In a study assessing both the immediate and sustained effect of triclosan and chlorhexidine for use as a hand wash preparation, Bartzokas *et al.* (1987) concluded that whilst both triclosan and chlorhexidine inhibited *Staphylococcus epidermidis* for up to four hours on a gloved hand, triclosan was found to be significantly better on an ungloved hand. However, a later study undertaken by Ayliffe *et al.* (1988) which compared the efficacy of a variety of agents including triclosan, chlorhexidine and povidone iodine concluded that, whilst povidone iodine and chlorhexidine were more effective than non medicated soap, triclosan was only marginally superior. In the same study the authors concluded that

chlorhexidine had a superior residual effect in comparison to triclosan. A later study by Bettin *et al.* (1994) compared the ability of 4% chlorhexidine gluconate in 4% alcohol with that of liquid soap to remove *Clostridium difficile* from both gloved and ungloved hands, supports the use of either soap or chlorhexidine as a handwash to remove *Clostridium difficile*. They concluded that there was little difference between the action of soap and chlorhexidine on residual bacterial counts. They also found that when tested on a gloved hand residual counts were lower following washing with soap than chlorhexidine. It should be noted that this study did not include triclosan for evaluation. Another study by Simpson *et al.* (1994) compared the efficacy of 4% chlorhexidine gluconate, 4% chlorhexidine gluconate with an emollient and povidone iodine with a non-medicated soap. They concluded that the three antibacterial agents were significantly better than the non-medicated soap using a gloved hand technique. Huang *et al.* (1994), in their study assessing the ability of chlorhexidine, liquid soap and povidone iodine, to remove MRSA from experimentally contaminated finger tips found that, whilst povidone iodine was superior to soap (with a clearance rate of 99.2% compared to 96.1% with soap), chlorhexidine was only marginally more effective than soap (clearance rate 97.2%).

The ability of antibacterial agents to display a good residual effect can be significant in the care and management of patients found to be colonised with MRSA.

Published guidelines relating to the management of MRSA patients advise the use of antibacterial agents to reduce skin colonisation (Duckworth *et al.*, 1990; Ayliffe *et al* 1998). Several studies have been undertaken to assess the residual effects of antibacterials. Bendig, (1990) demonstrated that both chlorhexidine and triclosan had a prolonged effect when compared to non-medicated soap. Faoagali *et al.* (1995) reported no statistically significant difference between chlorhexidine, triclosan or liquid soap on MRSA skin colonisation immediately following handwashing. However, a later study by Faoagali *et al.* (1999) comparing the efficacy of antibacterial agents, namely 4% chlorhexidine gluconate and 1% triclosan as a handwash on an acute ward, using both MRSA and coliforms as test organisms concluded that both agents were effective in reducing the total bacterial counts. Whilst the study by Faoagali *et al's.* (1999) concluded that chlorhexidine gluconate was more effective than triclosan in reducing total counts, triclosan was observed to have a significantly better ability to reduce the numbers of MRSA while chlorhexidine gluconate was found to be more effective on Gram-negative bacilli.

Other studies reviewing pre operative surgical hand disinfectants have focussed on the ability of antibacterial agents to affect the levels of skin colonisation. Bendig (1990), in a study undertaken on twenty healthy volunteers compared the effects of chlorhexidine, triclosan and non-medicated soap as a surgical hand disinfectant found that whilst chlorhexidine was more effective than non-medicated soap, a proportion of volunteers developed skin irritation when triclosan was used.

When assessing the acceptability of skin disinfectants the potential for adverse reactions must be considered. Studies by Webster (1992) to assess user acceptability of chlorhexidine gluconate 4% and triclosan 1% found that a proportion of individual patients complained about the drying effects of chlorhexidine, favouring the use of triclosan. A wider review of the literature to assess side effects when using chlorhexidine and triclosan have found that a few isolated cases of adverse reactions have been reported when chlorhexidine preparations have been used (Cheung and O'Leary, 1985; Evans, 1992), which brings into question its suitability for long term use.

Although few studies have been conducted in a clinical environment several *in vitro* studies have been undertaken to assess the effects antibacterial agents have on reducing or eradicating MRSA. McLure and

Gordon' (1992) assessed the activity of chlorhexidine and povidone iodine against 33 clinical isolates of *S.aureus* resistant to methicillin and found a noticeable difference in the behaviour of agents used. They concluded that povidone iodine was more effective than chlorhexidine, which they believed to have had minimal effect. Whilst these studies suggest that povidone iodine may be better as a hand disinfectant, when considering use of povidone iodine as a body wash, user acceptability is an important issue. Another key issue is iodine's ability to cause skin irritation and it is often recommended that patch testing is carried out prior to use.

Other *in vitro* studies have been undertaken to assess the effectiveness of chlorhexidine using povidine iodine as a comparative agent. Yasuda *et al.* (1993) assessed the bactericidal activity of four disinfectants and found similar findings to those of Mclure and Gordon (1992) which demonstrated that while povidine iodine was more effective, there was considerable variation in the duration of bactericidal activity of chlorhexidine. However, work by Sakuragi *et al* (1995) assessed the bactericidal activity of povidine iodine (10%) chlorhexidine gluconate (0.5%) and chlorhexidine (0.5%) in 80% ethanol on selected strains of both MRSA and MSSA. In their study, the authors concluded that whilst chlorhexidine in 80% ethanol was significantly more effective on

S.aureus, there as no significant difference between 10% povidone iodine and 0.5% chlorhexidine gluconate.

The majority of studies to assess the performance of antibacterial agents to reduce the levels of skin colonisation have been undertaken using the hand and glove methods. Some workers have studied the specific ability of a single application of antibacterial skin disinfectant to reduce the level of skin colonisation. A cross centre study by Ayliffe *et al.* (1983) comparing the efficacy of chlorhexidine and non medicated soap in the prevention of post operative wound infections on 5536 patients found a single application of chlorhexidine was of questionable effect. A previous study by Davis *et al.* (1978) assessing the ability of skin disinfectants in the reduction of potential pathogens on the abdomen of healthy volunteers found a reduction in the number of organisms present when chlorhexidine was used. In this study non-medicated soap was not used as a comparison, as the control agents used were either water or no treatment.

Several studies have been undertaken to assess the efficacy of antibacterial agents in the reduction of organisms from specific sites. Few studies have been reported which have demonstrated the sole use of antibacterial agents to either reduce or eradicate skin colonisation from patients found to be colonised with MRSA in the clinical environment.

Studies by Bodey and Rosenbaum (1973) and Bartzokas *et al.* (1984) identified triclosan as advantageous in the control of patients found to be positive with MRSA during an outbreak. O'Keefe *et al.* (1985) contest their findings, arguing that the reduction in those patients newly identified as MRSA positive was primarily attributed to strict infection control practices to include the isolation of patients and not body washes. Blumber and Klugman (1994) support the work of O'Keefe *et al.* (1985). In a review of an MRSA outbreak of 88 patients, they found that while the introduction of antiseptic bathing and the use of nasal creams was beneficial in reducing MRSA they also attributed a significant role to the isolation of patients. Other studies, by Tuffnell *et al.* (1987); Brady *et al.* (1990); Webster *et al.* (1994) and Zafar *et al.* (1995) using antibacterial skin disinfectants in the control of an outbreak of MRSA demonstrated that, where antibacterial agents have been used as either a body wash for patients or as a hand wash for staff, a reduction in the levels of MRSA and newly-colonised patients was found. However, it can be argued that while antibacterial agents have an effect, other contributing factors should be considered as being influential. These include the implementation of clearly defined infection control measures e.g. handwashing; heightened awareness of staff to the possible causes and prevention of cross infection and a reduction in the length of time of antibiotic therapy (Brady *et al.* 1990). Other studies undertaken specifically to assess the effectiveness of antibacterials on skin flora have been aimed at neonates and maternity

units and relate to the use of hexachlorophane (Gillespie *et al.*,1958; Pleuckhahn and Banks, 1963; Gezon *et al.*, 1973). However, work by Sarkany and Arnold, (1970) found that whilst hexachlorophene suppressed the levels of *S.aureus* on specific sites, namely axilla and groin, it appeared to encourage growth of organisms such as *Proteus*. The potential to select other organisms is an important factor which needs to be considered when using disinfectants since, in an attempt to eradicate one organism there is a potential to encourage proliferation of others.

Whilst antibacterial skin preparations are frequently used in the management of MRSA patients', consideration must be given to the use of both topical and systemic antibiotics. These are used either to reduce skin colonisation, as seen in chronic wounds such as leg ulcers, or to treat clinical infections such as wound infections or bacteraemia. Several studies have been reported which assess the effectiveness of antibiotic usage for patients with MRSA. However, as with antibacterial skin disinfectants, few studies have been identified which assess the effects that the use of antibiotics (either topical or systemic) have on the eradication of MRSA from the body surface of patients found to be colonised with MRSA.

Studies by Ward *et al.* (1981), Winn *et al.* (1980) and Yu *et al.* (1986) have shown a reduction in the levels of nasal colonisation with MRSA by 100% and between 66%-81% for extra nasal sites. They also demonstrated that neither topical bactroban nor intravenous vancomycin had an impact on nasal carriage of MRSA. They found that while oral rifampicin influenced the initial nasal carriage rate, a high percentage of nasal carriers became recolonised within 3 months. Similar findings were also identified by Watanakunakon *et al.* (1995) supporting the previous authors. Other studies by Smith *et al.* (1987); Smith and Kennedy, (1988); Rahman *et al.* (1988); Cookson, (1990); Cookson, (1998); Ambler and Drabu, (1996), have demonstrated antibiotic resistance, particularly to mupirocin, which is frequently used to treat nasal carriage of MRSA highlighting the need for caution with its use.

1.7. Risk Factors

It can be argued that controlling the levels of skin colonisation is advantageous, not only to reduce the risk of a clinical infection, but to reduce the potential environmental load of MRSA. Patients are often carriers of MRSA, i.e. colonised without having signs or symptoms of infection such as pyrexia, cellulitis or inflammation. However, some individuals with skin conditions such as eczema or psoriasis may shed large amounts of skin scales and disperse large numbers of the organism present on the skin scales into the environment. Therefore, if colonised

or infected with MRSA they can pose a potential hazard to more susceptible patients particularly patients with open wounds who are immuno compromised.

Patients with known skin conditions who are colonised with MRSA are often discouraged from using antibacterial agents as a body-wash to reduce the risk of hypersensitivity and prevent further drying and irritation to the skin. Therefore, patients with skin conditions found to be colonised with MRSA are encouraged to continue with their own skin care regime and not use antiseptics in the belief that once the condition of their skin has improved the levels of MRSA skin carriage would be reduced. This begs the question that if antibacterial skin disinfectants are not recommended on patients with known skin conditions why do we use antibacterial agents on patients potentially less likely to disperse large numbers of the organism into the environment?

Several studies have highlighted risk factors associated with acquisition of infections whilst in hospital. Haley *et al.* (1985) suggest four specific risk factors for post operative infection. They are: three or more underlying diagnoses; operations involving the abdomen; operations lasting longer than 2 hours and contaminated or dirty wounds. A later study be Garibaldi *et al.* (1991) asserts predisposing factors such as chronic bronchitis and smoking in the respiratory patient and underlying

diseases e.g. diabetes or long term steroid therapy resulting in immuno-suppression. Bibby *et al.* (1986), whilst supporting the views of Garibaldi *et al.* (1991), proposed that technology should highlight predisposing factors for infection, and suggest that a computer model corrected for age, gender, type of operation and would drainage in surgical patients would be of benefit in identifying patients at risk. While Ayliffe *et al.* (1992) do not disagree with the previous authors they contend that more work is required to define a model which would enable easy access to information. A recent National study carried out by Infection Control Teams throughout the United Kingdom into the prevalence of infection in hospitals attempted to investigate the significance of predisposing conditions in relation to hospital acquired infection. The same study also identified that 10% of the patient population had a hospital acquired infection (Thompson and Smyth, 1996). While studies have been undertaken to assess the efficacy of antibacterial agents and their ability to reduce/eradicate skin colonisation, few studies have been undertaken which consider external factors such as a patient's general health, skin condition or any immuno suppressed state.

1.8. Litigation

Another element for consideration is the increasing threat of litigation for Hospital Trusts as a result of patients acquiring infections. Kainitz and Kainitz (1992) support this view, inferring that there is a trend for society

to have an increased appetite for litigation. They suggest that patient's expectations have grown with the sophistication of medical practice and that these synergistic trends have expanded legal liability related to nosocomial or hospital acquired infection. Liability for nosocomial infections may be imposed on any health care provider including hospitals, doctors or nurses (Creighton, 1980) if it can be demonstrated that an infection occurred as result of a breach in the standard of care i.e. National or Hospital guidelines were not adhered to (Fifer, 1981).

1.9. Conclusion

From a review of the literature to evaluate the effectiveness of antibacterial agents namely: chlorhexidine gluconate 4% and triclosan 2% it can be concluded that within heath care establishments antibacterial agents are commonly used in skin washes both as a handwash preparation and as a body wash on patients found to be MRSA positive. It can also be inferred that the ability of organisms to be successfully removed from hands may largely be influenced by a proficient effective handwash technique as opposed to the efficacy of particular antibacterial agents. Therefore, when considering the use of antibacterials/ antiseptics as a treatment for MRSA, it can be argued that the key point is not necessarily what the patient is washed in but the procedure used to apply the solution.

Since the emergence of MRSA several attempts have been made to reduce or eradicate the levels of skin colonisation by using a variety of antibacterial (antiseptic) skin preparations for bathing such as chlorhexidine and triclosan and/or topical antibiotics such as mupirocin. The emergence of antibiotic resistance has been a focal point on many agendas. Discussions have taken place relating to the inappropriate prescribing of antibiotics both in humans and in veterinary circles. However, while guidelines issued for the control and prevention of spread of this potential pathogen have been produced their implementation has had limited success (Mulligan *et al.*, 1993; Marples and Reith, 1992; Farrington *et al.*, 1990). A recent report by the Standing Medical Advisory Committee (SMAC) - 'The Path of Least Resistance' (1998) highlights the problems associated with the misuse of antibiotics as a major factor in the emergence of resistant micro-organisms. The report identifies specific factors that have had an effect on resistance such as antibiotic prescribing, surveillance, hygiene of infection control practices, veterinary and agricultural use and education. In recent years we have seen anti-bacterials used in a variety of preparations from cosmetics to non-food items like chopping boards, disinfectants. The liberal use of these agents has to be considered as a factor in the future emergence of resistance.

In conclusion, the published literature shows that there is a wide range of antibacterial agents which are in use to help reduce or eradicate MRSA skin carriage, and have variable effects on the level of skin colonisation. Of those studies investigated the use of hand disinfectants to reduce or eradicate MRSA hand colonisation, povidine iodine is favoured with little evidence being present to suggest that chlorhexidine or triclosan are better or worse. The efficacy of both triclosan and chlorhexidine in the reduction or eradication of MRSA skin colonisation in patient's requiring hospitalisation is still a matter of conjecture and debate. Therefore, while no statutory guidelines are evident, and in view of few studies being undertaken specifically aimed at reviewing the effects of antibacterials on patients found to be MRSA positive in a clinical environment, this project took the form of a controlled study using two of the currently recommended agents (chlorhexidine 4% triclosan 2%) and a non medicated soap in the treatment of MRSA colonisation.

2. MATERIALS AND METHODS.

2.1. Introduction

The study comprised a comparative randomised trial of three agents used as body washes for the reduction/eradication of the level of MRSA skin colonisation in patients known to be MRSA-positive. The agents used were triclosan (the existing treatment used at City Hospital, Birmingham), chlorhexidine gluconate (used in other centres) and soap solution.

2.2. Aim

The aim of the study was to compare the effectiveness of the two designated antibacterial agents with the soap solution as a control.

2.3. Research site

City Hospital NHS Trust.
Dudley Road.
Birmingham.B18 7QH

Aston University
Aston Triangle
Birmingham.B4 7ET

2.4. Initial contact with professional bodies

- Medical Directorate and Service Managers were contacted to obtain consent to undertake the study on their wards.
- To ensure staff co-operation and understanding all participating wards were visited and meetings arranged with both the ward managers and staff to discuss the implication of the study for staff and patients.

- Ward Meetings were followed up with written documentation to reiterate the nature of the study (see appendix 1)

2.5. Ethical factors

- Patients formed the study group.
- The randomisation of agents being used to compare the effectiveness of antibacterial agents meant that not all patients received the current topical treatment regime (triclosan).
- All agents used (soap, chlorhexidine gluconate and triclosan) are all currently licensed products and used within health care establishments.

Informed written consent was obtained from all patients entering the study and written information relating to the nature of the study and MRSA was given to them all patients commenced on any of the three variables. Ethical approval was sought and granted by the Ethical Committees at both Coventry University (Pilot study undertaken as part of BSc (Hons) Health Sciences) and City Hospital NHS Trust.

2.6. Study Design

A randomised controlled experimental design involving 3 variables.

2.6.1. Agents used

i. Triclosan 2% w/v (Aquasept, Seton Healthcare Group, Oldham, UK), currently the treatment of choice for the

reduction or eradication of MRSA skin colonisation at City Hospital, Birmingham.

ii Chlorhexidine gluconate 4% w/v (Hydrex, Adams Healthcare, Leeds, UK), used in other UK centres for the reduction or eradication of MRSA skin colonisation and as a handwash in designated areas.

iii Soap (liquid) - (Cutan Gentle-wash, Deb Ltd., Belper, UK.) was an approved product, used as a control. Note that this soap formulation exerted some antimicrobial activity due to the presence of bronopol as a preservative.

NB: As part of the existing hospital protocol, patients identified as MRSA positive on nasal swabs were commenced on Mupirocin nasal cream, twice daily for 5 days. Two courses were usually advocated. If nasal colonisation persisted two further courses of chlorhexidine (Naseptin) were given for five days. If there was no reduction in nasal colonisation, the patient was monitored for nasal carriage by regular microbiological swabbing.

2.6.2. Standardisation of treatment.

To ensure treatment was standardised throughout the trial, 10 millilitres (mls) of each solution (chlorhexidine, triclosan and soap) was decanted into individual universal containers over a 5 day period.

2.6.3. Advantages of standardising the treatment.

- Trial products presented in the same format, reduced patients' preference.
- Standardisation of the volume used ensured all trial subjects received the same amount of solution. Pre-set volumes ensured that the required amount was used. This prevented too much being used, reducing the potential for dryness and irritation of the skin which could potentially increase the level of skin colonisation and therefore influence the validity and reliability of the results. If too little was used, this may have affected the concentration of triclosan and chlorhexidine present on the skin to kill the organism. This may have influenced the effectiveness of the antibacterials to reduce the levels of MRSA on the skin surface potentially compromising the validity of the results.
- All patients were washed using the same technique.
- Patients were randomised from different specialities e.g. medical, surgical, orthopaedic elderly care.
- Microbiological screening was undertaken within a set time period following one course of treatment.
- All microbiological samples taken were processed in accordance with laboratory protocols.

2.7. Reduction of bias

In order to reduce the possibility of bias the following procedures were instituted:

- The agents used as a body wash during the trial was randomly selected by an independent person.
- Sealed, unlabelled envelopes containing the chosen treatment (e.g. triclosan, chorhexidine or soap solution) was left with each ward manager.
- Once a patient had agreed to enter the trial, an envelope was selected by a staff member at ward level. Once selected the envelope was opened and the treatment identified.
- Identification of MRSA was undertaken by the Microbiology Department and the Hospital Infection Research laboratory and not the researcher.
- Those companies which produce triclosan, chlorhexidine and the soap solution were not contacted for sponsorship.
- All products used for the controlled randomised trial were presented in the same format.

2.8. Sample group

2.8.1. Recruitment

Because no information was available to predict the performance of triclosan and chlorhexidine in the eradication or reduction of MRSA, it was not possible to carry out a power calculation for the

patient number. The initial aim was to recruit 150 patients into the study to allow sufficient numbers to be assessed. This figure was variable due to the unpredictability of the patient's length of stay in hospital and inclusion criteria to enter the randomised control trial.

Any patient admitted to City Hospital NHS Trust who had microbiology specimens processed positive for MRSA was considered for entry into the trial.

2.9. Inclusion to the study

Any patient admitted to City Hospital NHS Trust identified as positive for MRSA from microbiological sampling obtained from:-

- Clinical specimens
- Admission screens
- Ward Screens

2.10. Exclusion from the study

- Patients with known skin conditions e.g. eczema
- Patients known to be MRSA positive who had had topical treatment in the previous two weeks.
- Patients with known or suspected allergies to anti-bacterial agents.
- Patients unable to speak or understand English.
- Patients non compus-mentis.

- Patients on systemic antibiotics (withdrawn from inclusion criteria following Pilot study).

2.11. Withdrawal from the study

- Reaction to antibacterial agents used in the study.
- Patients no longer wishing to participate in the study.

2.12. Process used to allocate the trial agents.

Samples were allocated by an independent body. Equal numbers of colour coded treatment sheets (see appendix 2,3,4) were placed in sealed envelopes with no means of identification on the front. Each patient was randomly allocated a topical treatment regime.

2.13. Documentation used for the trial

2.13.1 Staff

- Information sheets were given to all participating wards explaining the reason for the research the aims and objectives of the study, staff involvement and instructions relating to the research protocol (see appendix 1).
- Colour coded information sheets identifying the allocated skin agents to be used were issued to all staff for each individual patient. Each sheet contained the following information:
    - Date treatment was to be commenced
    - Date treatment was to be discontinued
    - Type of agent to be used

- Rescreen date
- Section to report any adverse skin reactions to agent used (see appendix 2,3,4).

2.13.2. Patients

Leaflets were given to all patients explaining the followiing:

- The nature of the study (see appendix 5)
- What MRSA is (see appendix 5,6)

A written consent form was obtained form all patients entered in the controlled randomised trial to confirm both their understanding as to the nature of the research and their willingness to participate in the study (see appendix 7).

2.14. Study procedure

- Patient admitted to a ward
- Microbiological samples were requested if indicated from recognised pre designated sites to include:-
  (i) Nose, groin and lesion swabs - upon detection of a positive isolate taken as a clinical specimen or ward screen prior to commencement of treatment.
  (ii) Nose, groin and lesion swabs - from all known MRSA patients on readmission to ascertain their present MRSA status.

2.14.1. Action following identification of a positive result for patients inclusion into the randomised control trial

Patients were approached on an individual basis, an explanation regarding their MRSA status and nature of the study was given. If the patient consented to take part in the study a written consent was obtained (see appendix 7) and the patient was randomly allocated one of the three designated agents to use for a period of 5 days and a proforma completed (see appendix 8).

2.14.2. Application of agents used

All agents used were in a liquid formulation and applied as a lotion. Staff were advised to wet the surface of the skin with warm water, then using a soft disposable cloth apply 10mls of the allocated agent (supplied in a universal container) to the whole body avoiding the eyes . The skin was then rinsed with warm water and dried.

2.15. Rescreening

Treatment was discontinued after 5 days, a period of 48 hours was left prior to rescreening for each patient. Specimens were taken to include: nose, groin, lesion swabs, contact plates of buttocks and finger plates (catheter specimen of urine. and sputum specimens were advised if applicable)

2.16. Identification of *S.aureus*

MRSA isolates was confirmed by the Microbiology Department (to include the Hospital Infection research Laboratory) and Microbiology Department) at City Hospital NHS Trust. All strains obtained from patients known to be MRSA positive were stored within the laboratory on agar 'slopes'. A selected number of strains were phage typed at the Central Public Health Laboratory, Colindale, London, UK.

S.aureus was isolated by means of standard culture methods, appropriate for the specimens received. Specimens were cultured on Phenolphthalein Diphosphate (PPD) agar plates. Plates were incubated at 37°C for 18 hours and examined. *Staph. aureus* was identified by standard microbiological methods. Once an organism was isolated sensitivity testing was performed using a Disk Diffusion Method following BSAC Standard Guidelines (BSAC,1998). Strains of *S.aureus* were tested against 'first line' antibiotics as follows: penicillin, erythromycin, vancomycin, gentamicin, fucidin and methicillin. Following confirmation of methicillin resistance, MRSA strains were further tested against the following second line antibiotics: rifampicin, trimethoprim and mupirocin.

2.17. Preparation for determining the MICs for trial agents used

2.17.1 Preparation of plates for MICs

i. The chosen media for agar plates was Mueller-Hinton agar (Oxoid Ltd., Basingstoke, Hampshire, UK) containing (g/L).

ii. A 500 mls volume was made by mixing 19 g of Mueller Hinton agar with 500mls of water.

iii. The mixed solution was autoclaved at 121°C for 15mins and cooled to 50°C.

iv. Pre calculated amounts of chlorhexidine, triclosan or soap were added to universal containers to give the desired concentration (see 2.17.2).

v. 20mls of agar was added to universal containers to ensure solution mixed prior to pouring pre measured doses onto plates.

2.17.2. The concentrations of the agents in the poured plates ranged from 0.005 to 16 μg/ml in doubling dilutions.

2.17.3. Strains were cultured for 18h on Mueller Hinton agar plates at 37 °C, checked for purity by colonial appearance. Individual colonies were resuspended in saline to a density of 10^8 cells/ml determined by measuring the absorbance at 500nm. Previous calibrations determined that an absorbance of 1.0 was equivalent to a cell density of 10^8 cells/ml. The suspension was diluted 1:100 in Mueller Hinton broth containing 10^6 cells/ml.

2.17.4. Cell suspensions prepared from 36 different strains were dispensed into wells of a sterile microtitre plate. A multipoint inoculator was then used to transfer approximately 0.01ml of each suspension to the surface of the Mueller Hinton agar plates containing the range of disinfectant or soap solutions. The number of cells transferred to the plates in each inoculum spot was 10^4 cells.

2.17.5. The inoculated plates were incubated for 18h at 37°C and the MIC recorded as the minimum concentration of the agent present in the plate which inhibited colony formation.

2.18. Pulsed Field Gel Electrophoresis (PFGE)

10 isolates were selected and examined by PFGE. The MRSA isolates were chosen as representatives of isolates with low, medium and high levels of resistance to each of the agents used. Time restrictions meant that not all isolates could be examined.

2.18.1. Preparation of agarose blocks

- Cells were incubated overnight aerobically in Mueller Hinton infusion broth, (Oxoid, Basingstoke) in shake flasks at 37°C.
- The cells were pelleted by centrifugation (Eppendorf microfuge, 13,500 rpm, 5min) and then resuspended in Net-100 (0.1M NaCl, 0.1M EDTA, 0.01M Tris-HCl pH 8.0) to yield a cell suspension of 20mg/ml wet weight.

- Cells were then mixed using equal volumes of 0.9% chromosomal agarose (BioRad, California) and poured into a perspex mould and allowed to set.
- The agarose blocks were then be incubated at 37°C for 24 hours in a 3 ml lysis solution containing (6mM Tris-HCl pH 7.6, 1M NaCl, 100mM EDTA pH 8.0 + 0.5% N-lauryl-sarcosine) + 4μl lysostaphin (66 units/ml, Sigma, St. Louis, USA).
- The lysis solution was replaced with 3 ml of ESP (0.5M EDTA pH 9.0, 1% N-lauryl-sarcosyl, 1.5mg/ml proteinase K (Sigma) and blocks incubated for 48 hours at 50°C.

2.18.2. Pre- digestion treatment

- Blocks were washed twice in 5ml TE (25mM Tris-HCl pH 8.0) containing

  30 μl of 1mM PMSF on a slow roller for 2 hours.
- Blocks were then washed with three changes of TE (Tris-EDTA).

2.18.3. Digestion of Blocks

- Agarose blocks were cut to a thickness of 1mm, equilibrated in 200μl of restriction digest buffer (Boehringer Mannheim, Germany.) on ice for 15 mins.
- New buffer was be added along with 40 units of restriction enzyme, *sma1* (Boehringer Mannheim, Germany) equilibrated on ice for 15 mins and incubated at 30 °C overnight.

- The enzyme buffer was then replaced using a 200 μl ES solution (0.5 M EDTA pH 9.0, 1% N-lauryl-sarcosine) and heated at 50°C for 15 minutes.
- Slivers were then washed with 1 ml TE and left for 15 mins before loading onto the gel.

2.18.4. Electrophoresis of Samples

- Samples were loaded into the gel, 1% molecular biology grade agarose (Bio Rad, California) in 0.5 x TBE (90mM Trisborate, 0.5M EDTA pH 8.0) and sealed in molten agarose. Lambda concatamers (Bio-Rad, Richmond, USA) were used as molecular size standards.
- The gel was then placed into the electrophoresis system (CHEF DRIII, Bio - Rad) containing 2 litres of pre cooled 0.5 x TBE.
- The buffer was cooled to 10°C and pumped continuously around the system at a rate of 11/min. A constant voltage of 6 V/cm was applied with an increasing pulse time of 10 -16 sec, for 22 hours.

2.18.5. Staining of the gel

- The gel was stained in 2.5 μl of 10 % ethidium bromide in 200 ml of distilled

  water for 30 min.
- The gel was then washed in 200ml of distilled water for 1hr 30 min.

- The gel was then observed under a UV light and the image recorded using the 'grab it' software (UV Products Ltd., Cambridge, UK).

2.18.6. Interpretation of Pulsed Field Patterns

Analysis of fragment patterns was carried out by the definitions and criteria used by Tenover *et al.* (1995). The size and number of fragments in each isolate were identified. Isolates were compared to determine any genetic or epidemiological similarities, as defined below:

Indistinguishable: isolates were considered to be genetically indistinguishable if they had the same number of bands, the corresponding bands were in the same position and of the same size.

Closely related: patterns differed from the predominant strain by a single genetic event, a point mutation, or deletion of DNA. This manifested as two or three band differences.

Possibly related: patterns differed from the predominant strain by two independent genetic events. These were observed by four to six band differences. These Isolates may have had the same genetic lineage but were less likely to be epidemiologically related.

Unrelated: patterns differ by three or more independent genetic events. These were observed by seven or more band differences.

Genetic events

- Point mutation: resulting in the loss or gain of a restriction site
- Insertion of DNA into an existing restriction fragment.
- Deletion of DNA from a fragment.

NB. Tenover *et al.* (1995) recommended the above guidelines when comparing strains over one to three months. The stains used in the study all exceeded this period. Statistical analysis was not possible due to time restrictions and sample size.

2.19. Data Collection

Agents used.

A pre-devised proforma (see appendix 8) was used for all patients entered in the study to enable standard collection of baseline data to be obtained from all patients and allow comparative analysis of data from patient in controlled randomised trial.

Demographic data was collected from both category and descriptive information. Data obtained from specimens was recorded as 'positive' and 'negative'.

2.20. Data Analysis

i. The statistical significance was measured using the 'Chi-square' or 'extended Chi-Square' test (with Yates correction in the event of smaller numbers) (Polit and Hungler, 1991) and Fisher Exact Test.

ii. Descriptive data was analysed from age, mean age was calculated by analysing percentages/numbers in each category.

iii. Microbiological screening results were analysed by evaluating the total numbers of positive and negative results pre- and post-treatment by percentages.

iv. Resistance to triclosan, chlorhexidine and soap was evaluated qualitatively.

3. RESULTS

The planned sample size was 150 patients. However, due to the specific inclusion and exclusion criteria, together with the overall length of stay for patients remaining in hospitals decreasing the final recruitment size was 96. Of those:

- 5 patients were discharged either home or into care in the community prior to completing one course of treatment.
- 1 patient died with conditions not related to their MRSA status prior to completing one course of treatment.
- 9 patients were excluded from the screening results, as they were identified as MRSA positive on nasal swabs only.

The final sample size was 81.

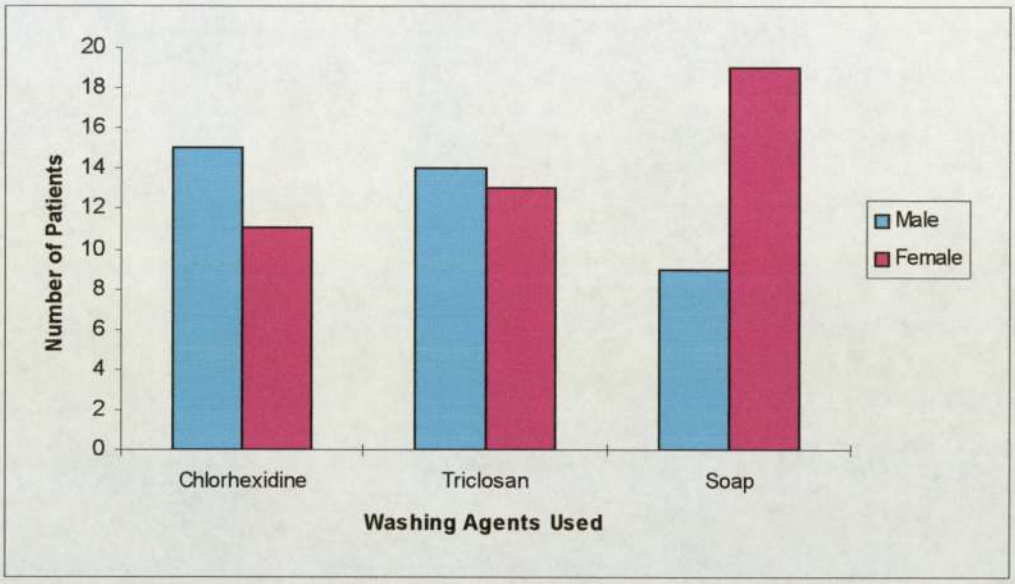
Since the final sample size was reduced it was decided in this instance to evaluate patients who had completed one course of treatment.

The sample size was too small to do any parametric statistics. Therefore data was processed descriptively.

Whilst the numbers were too small to demonstrate any statistical significance, it can be seen from the findings, that of the 81 patients entered in the trial, random allocation of the three variables did not result

in any disproportionate groups, with 32% receiving chlorhexidine, 33% triclosan and 35 % soap.

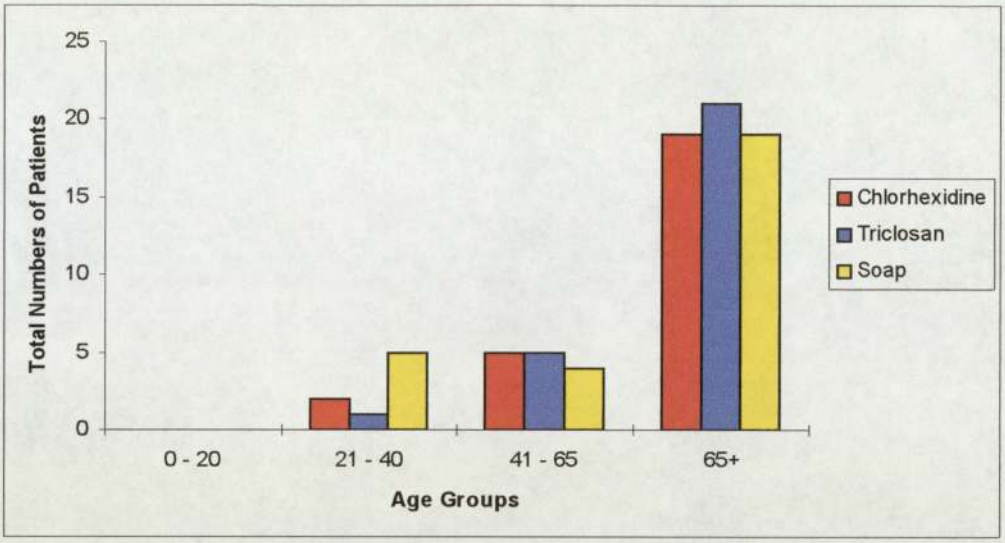
3.1. Gender



3.1.1. Chart to Illustrate the total numbers of patients entered into the study by Gender

Of the 81 patients entered into the study, the above chart illustrates that there were proportionally more female patient's (43) than male patient's (38). The gender mix in each group was more even in the triclosan and chlorhexidine groups in comparison to those patients who were allotted soap.

3.2. Age groups



3.2.1. Chart to Illustrate the age range of patients entered into the study

Minimum	**23 years**
Mean	**71.4 years**
Maximum	**98 years**

3.2.2. Table to illustrate the minimum, mean and maximum age values

It can be seen from the above chart that whilst no patients in the study were between 0 -21 years, the minimum age was 23 years with the maximum age 98 years. The majority of patients (73%) both male and female entered into the study were in the age group 65 years plus, indicating a broad spectrum of patients colonised with MRSA.

3.3 Speciality Groups

	SPECIALITY GROUPS (by Directorates)				
	Medical	Surgical	Orthopaedics	Elderly Care	Total
Chlorhexidine	12	3	6	5	26
Triclosan	10	8	6	3	27
Soap	10	4	8	6	28
Total	32	15	20	14	81

3.3.1. Table to illustrate the total numbers of patients by speciality groups.

The above table demonstrates that the majority of patients (39.5%) included in the study were from the Medical Directorate, with 24.7 % from Orthopaedics, and 17.3 % from Elderly Care. Whilst only 17.2% of patients were in Elderly Care, the presence of 71.6% of patients over the 65 years of age indicates that the latter groups of patients were dispersed across the speciality groups.

3.4. Antibiotic Therapy

Positive screen results						
	Vanc.	**β.Lact**	**Ceph.**	**4. Quin.**	**Others**	**No Antibiotics**
Chlorhexidine	-	5	2	-	-	13
Triclosan	-	3	2	-	-	12
Soap	2	3*	2*	-	3	10
Negative screen results						
	Vanc	**β.Lact**	**Ceph.**	**4. Quin.**	**Others**	**No Antibiotics**
Chlorhexidine	-	-	1	1	-	4
Triclosan	1	3	1	-	-	5
Soap	2	1	1	-	-	6
Overall Total	**5**	**15**	**9**	**1**	**3**	**50**
2 patients of which 1 was commenced on a Cephlosporin and β. Lactams 1 was commenced on a Cephlosporin and Metronidazole						

3.4.1. Table to illustrate the numbers of patients in each group on antibiotic therapy

Key Vanc. = Vancomycin
β. Lact = β. Lactams
Ceph = Cephalosporins
4. Quin = 4. Quinolones

NB: Note all patients identified as having positive nasal carriage were commenced on a 5 day course of topical mupirocin twice daily as per Trust Policy.

3.5. Antibiotic therapy vs. negative screening results

The table below illustrates a correlation between the numbers of patients commenced on antibiotic therapy and the number of patients who obtained a negative MRSA screen 48 hours post-treatment with a designated body wash.

	Chlorhexidine	Triclosan	Soap
Number of patients with negative MRSA screen results	6	10	10
Total number of patients commenced on Antibiotic Therapy	9	10	14

3.5.1. Table to illustrate a comparison of the total number of patients on antibiotics vs. negative screens

Whilst the numbers presented are too small to obtain any statistical significant data, there was little difference between the clearance rate of MRSA skin colonisation and antibiotic therapy.

3.6. Comparison of positive and negative screen results

	Chlorhexidine	Triclosan	Soap	Total
Positive Screen results 48 hrs. Post washing	20	17	18	55
Negative Screen results 48 hrs post washing	6	10	10	26
Total	**26**	**27**	**28**	**81**

3.6.1. Table to identify the numbers of patient's both negative and positive for MRSA following one course of body washes

Of the 81 patients entered into the study, the percentage of patients found to be negative following one course of treatment for each of the three variables used was as follows:

- Chlorhexidine 23%
- Triclosan 37%
- Soap 36%

Triclosan (at 37%) was marginally better than soap (at 36%), which in turn was better than chlorhexidine (at 23%) at reducing the levels of skin colonisation of MRSA. However, the sample group was too small to be of statistical significance.

ID Number	Positive sites prior to commencing body washes					Antibiotic Therapy	Screening Swab Results taken 48 hours following completion of one course of body washes				
	Nose	Groin	Buttocks	Fingers	Lesion/ other Sites		Nose	Groin	Buttocks	Fingers	Lesions/ Other site
8	-	-	-	-	Sputum Trache	-	Pos	Pos	-	-	Pos
13	-	-	-	-	Abdo Abscess	-	Pos	Pos	-	-	-
17	Pos	-	-	Pos	Pos Lesion	-	Pos	Neg	Neg	Pos	Pos
21	-	-	-	-	Pos - Toe	Ceph.	Pos	-	Pos	Pos	Pos-foot
22	Pos	-	-	Pos		Beta L.	Pos	-	-	Pos	-
27	Pos	-	-	Pos	Amputation	-	Pos	-	Neg	Neg	Pos
28	Pos	-	-	Pos		Beta L.	Pos	Neg	Neg	Pos	-
37	Pos	-	-	-	Pos - Cath	Beta L.	Pos	neg	-	-	-
45	Pos	Pos	-	Pos		-	Pos	-	Pos	Pos	Neg – hip
51	-	-	Pos	Pos	Rt. Hip (MSSA)	-	Neg	-	Pos	Pos	Pos (MRSA)
59	-	-	-	Pos	Sputum	Beta L.	Pos	-	Neg	Pos	-
65	Pos	-	Pos	-	Pos – wound	Ceph.	Pos	-	Neg	Pos	Urine- neg
71	-	-	Pos	Pos	Sputum	Beta L	Pos	-	Pos	Pos	-
80	Pos	Pos	-	Pos	-	-	Neg	-	Neg	Pos	Pos
82	Pos	-	Pos	Pos	-	-	Pos	-	Pos	Pos	Pos
83	Pos	-	-	Pos	Pos Lesion	-	Pos	Neg	Pos	Pos	Pos
85	Pos	-	-	-	Sputum	-	Neg	-	Pos	Pos	-
93	Pos	Pos	-	-	-	-	-	-	-	-	Sputum
94	-	Pos	-	-	Perianal	-	Pos	Pos	-	-	-
96	Pos	-	-	-	Lesion	-	Pos	Neg	-	-	Pos

3.6.2. Table to illustrate screening swab results of MRSA patients pre and post one course of body washes with Chlorhexidene

- = swabs not taken Pos = Positive, Neg = Negative.

ID Number	Positive sites prior to commencing body washes					Antibiotic Therapy	Screening Swab Results taken 48 hours following completion of one course of body washes				
	Nose	Groin	Buttocks	Fingers	Lesions/ other sites		Nose	Groin	Buttocks	Fingers	Lesions/ other sites.
7	Pos	-	Pos	-	-	-	Pos	-	Pos	Neg	Pos
12	-	-	Pos	-	Necrotic Calf	Beta lactam	-	Pos	-	-	-
14	Pos	Pos	-	-	Redivac	-	Pos	-	Pos	-	Pos
15	-	-	-	Pos	Sacral Lesion	Beta lactam	Pos	-	-	Pos	Pos
16	Pos	-	Pos	-	(MSSA)	-	Neg	-	Pos	Pos	Pos (MRSA)
18	-	-	Pos	-	-	-	Neg	Pos	Pos	Pos	-
23	Pos	-	-	Pos	-	Cephlosporins	Pos	-	Pos	-	Pos
24	-	Pos	-	-	CSU/elbow	-	Pos	Pos	-	-	Pos
31	Pos	-	Pos	-	lesion (MSSA)	-	Pos	-	Pos	Neg	Pos (MRSA)
32	Pos	-	-	Pos	-	-	Pos	-	Pos	Neg	-
35				Pos	W/S Ankle (MSSA)	-	Pos		Neg	Pos	Pos (MRSA)
38	Pos	-	Pos	Pos	-	-	Pos	-	Pos	Pos	-
52	-	Pos	-	Pos	-	-	Neg	-	-	Pos	-
61	Pos	-	Pos	Pos	-	Beta lactam	Pos	-	Neg	Pos	-
62	-	-	-	-	Haematoma	-	-	Pos	-	Pos	Pos
67	Pos	-	-	Pos	-	-	Neg	-	Neg	Pos	-
92	Pos	-	Pos	-	CSU	Ciprofloxacin	Pos	-	Pos	-	-

3.6.3. Table to Illustrate screening swab results of MRSA patients pre and post one course of body washes with Triclosan

- = swabs not taken Pos = Positive, Neg = Negative.

ID Number	Positive sites prior to commencing body washes					Antibiotic Therapy	Screening Swab Results taken 48 hours following completion of one course of body washes				
	Nose	Groin	Buttocks	Fingers	Lesion/ other sites.		Nose	Groin	Buttocks	Fingers	Lesions/ Other sites
3	-	-	Pos	Pos	-	Vanc	Pos	Pos	Pos	-	-
4	-	Pos	-	-	Lesion (MSSA)	Vanc	Neg	Neg	-	-	Pos (MRSA)
33	Pos	-	-	-	hand lesion	-	-	-	Pos	Neg	Healed
41	Pos	Pos	-	-	-	-	Pos	Pos	-	-	-
49	-	Pos	-	-	Foot abscess. CVP Tip	Beta lactam Cephlosporin	Pos		Pos	Neg	Pos
53	-	-	-	-	Sputum, cvp, tip	-	Pos	Neg	-	-	Pos
58	Pos	-	-	-	Lesion	Beta Lactam	Neg	Pos	Pos	Pos	-
64	Pos	-	-	-	Pressure Sore	Beta Lactam	Pos	-	Neg	Pos	Pos-ankle
68	Pos	-	-	Pos	Rt. Hip (MSSA)	-	Neg	-	Pos	Neg	Pos (MRSA)
69	Pos	-	Pos	Pos	Urine	-	Pos	-	Pos	Pos	Pos
70	Pos	-	Pos	Pos	-	-	Pos	-	Pos	Pos	Pos - trache (MRSA)
76	Pos	-	Pos	-	-	-	Neg	-	Pos	Neg	-
77	Pos	-	Pos	-	-	Oxyteracycline	Neg	-	Neg	Pos	-
81	Pos	Pos		Pos	CVP line	Ceph. Metr.	Neg	--	-	Pos	Pos
84	Pos	Pos	-	-	Groin	Erythromycin	Pos	-	Neg	Pos	-
86	-	-	-	-	Lt. Foot	-	Neg	-	-	-	Pos
89	Pos	-	-	-	Rt. Ankle	-	Neg	-	Neg	Pos	Healed
91	-	-	-	-	CVP Tip/ trachae	-	Pos	-	-	-	Pos

3.6.4. Table to illustrate screening swab results of MRSA patients pre and post one course of body washes with soap solution.

- = swabs not taken Pos = Positive, Neg = Negative.

ID Number	Screening Swab Results prior to commencing treatment.					Antibiotic Therapy	Designated Body Wash	Screening Swab Results taken 48 hours following completion of treatment.				
	Nose	Groin	Buttocks	Fingers	Lesion			Nose	Groin	Buttocks	Fingers	Lesion
1	Pos	-	-	-	-	-	Chlor.	Neg	--	-	Neg	-
2	Pos	-	-	-	-	-	Chlor.	Neg	Neg	-	-	-
34	-	-	-	-	W/S knee	-	Chlor.	Neg	Neg	-	-	Neg
48	Pos	-	-	-	-	-	Chlor.	Neg	Neg	-	-	-
50	-	-	buttocks	-	-	-	Chlor.	Neg		Neg	Neg	-
95	Pos	-	-	-	-	-	Chlor.	Neg	Neg	Neg	-	-
25	-	-	-	-	PEG	-	Chlor.	Pos *	Neg	-	-	Neg
55	-	-	-	-	Lt. Foot	Ceph	Chlor.	Pos *	Neg	-	-	Neg – foot
63	-	-	-	-	Rt. Shin	4 Quin	Chlor.	Pos *	-	Neg	Neg	Neg – foot
90	-	-	-	-	Groin /Peri	-	Chlor.	Pos *	-	Neg	-	-
5	-	-	-	-	Ankle	-	NMS	-	-	-	-	Ankle
9	Pos	-	-	-	-	-	NMS	-	Neg	-	-	Neg
10	-	-	-	-	Eye	-	NMS	Neg	-	Neg	Neg	-
36	-	-	-	-	W/S knee	Ceph	NMS	Neg	-	Neg	Neg	Neg
39	-	-	-	-	Ankle	Vanc	NMS	Neg	Neg	-	Neg	Neg
54	Pos	-	-	-		Ceph	NMS	Neg	-	Neg	Neg	Neg
56	-	-	-	-	W/S	Vanc	NMS	Neg	Neg	-	-	Neg
72	-	-	-	-	Blood	-	NMS	Neg	-	Neg	-	-
43	-	-	-	-	Heel	-	NMS	Pos *	Neg	-	-	-
44	-	-	-	-	Leg Ulcer	-	NMS	Pos *	Neg	-	-	-

3.6.5.Screening Swab Results of MRSA Patient negative following one course body washes

- = swabs not taken Pos = Positive, Neg = Negative.

ID Number	Screening swab results prior to commencing treatment					Antibiotic Therapy	Designated Body Wash	Screening swab results taken 48 hours following completion of treatment				
	Nose	Groin	Buttocks	Fingers	Lesion			Nose	Groin	Buttocks	Fingers	Lesion
66	Pos	-	-	-	-	Beta L	NMS	Pos *	Neg	-	Neg	-
88	Pos	-	-	-	-	-	NMS	Pos *		Neg	Neg	-
11	-	-	-	-	Pelvic wound	Vanc	Tric.	Neg	Neg	Neg	Neg	-
26	-	-	-	-	Ulcer shin	-	Tric.	Neg	-	-	Neg	Neg
9	Pos	-	-	--	-	-	Tric.	Neg	Neg	-	-	-
40	Pos	-	buttocks	Fingers	-	Beta L	Tric.	Neg	Neg	-	-	-
46	-	-	-	-	Pin site	Beta L	Tric.	Neg		Neg	Neg	Neg
47	-	-	-	-	Sputum	-	Tric.	Neg	Neg			-
57	Pos	-	-	-		-	Tric.	Neg		Neg	Neg	-
73	-	-	-	-	Sputum	Ceph	Tric.	Neg	Neg		Neg	-
74	-	Groin	-	-	Groin	Beta L	Tric.	Neg	Neg	Neg	Neg	-
75	-	-	-	-	Bron. Lav.	-	Tric.		Neg	-	-	-
6	-	-	-	-	Rt. Hip	-	Tric.	Pos *	-	Neg	Neg	-
30	Pos	-	-	-	-	-	Tric.	Pos *	-	-	-	-
87	Pos	-	-	-	-	-	Tric.	Neg	Neg	-	-	-

*= Indicates those patients that were positive on nasal swabs following discontinuation of treatment but wound and lesion swabs taken were negative for MRSA.

3.6.5.(cont) Screening Swab Results of MRSA Patient negative following one course body washes

- = swabs not taken Pos = Positive, Neg = Negative.

It can be seen from the above tables (3.6.2–3.6.5) that, prior to commencement of treatment with mupirocin, 45 of the 81 patients entered into the trial were positive nasally for MRSA. Of these 45, 16 were negative for MRSA following one course of mupirocin. This would suggest that the use of mupirocin had little impact on clearing patients colonised with MRSA nasally. Follow up screening identified a further 20 patients positive for MRSA on nasal swabs.

	Screening results of lesions before washes	Screening results of lesions after washes
8	++	++
13	+	-
17	++	+++
21	+++	+++
27	+++	++
31	+/- MRSA	+ MRSA
80	+/-	+/-
82	-	Scanty (pressure sore)
83	++	++
96	++	++
7	-	++
14	+	+/-
13	++	+
16	+ MSSA	+++ MRSA (pressure sore)
23	+++	++
24	++	+++
31	+/- MSSA	++ MRSA
35	+/- MSSA	+++ MRSA
62	++	+/-
4	+ MSSA	+/- MRSA
49	+/-	+/-
53	+	+
64	++	++
68	+/- MSSA	+ MRSA
70	No Lesion	+++ MRSA (trachae)
81	++	++
80	+++	+
91	+	++

3.6.6. Table to illustrate screening results of lesion pre and post washing

It can be extrapolated from the above table that whilst the numbers were too small to be of statistical significance there was little difference between the growth of organisms pre and post washing. However it can also be seen that the 6 lesions identified as having MSSA pre washing were identified as MRSA post washes. Equally while one patient had no lesion initially, following screening swabs identified +++ growth of MRSA as a tracheal swab post washing.

3.7. Statistical Analysis

To determine whether there was any statistical significance between the three variables, data was analysed using the chi-square test and the Fisher exact test.

'Chi - Square' Test			
	Chlorhexidine	**Soap**	**Total**
Positive	20	18	38
Negative	6	10	16
Total	**26**	**28**	**54**
Chi - square statistic (with Yates correction) = 0.5154 with 1 degree of freedom. The two - sided P Value is 0.4728, considered not significant. There is not a significant association between rows and columns. Odds Ratio = 1.852 95% Confidence Interval; 0.5600 to 6.124. (using the approximation of Woolf)			

Fisher Exact Test			
	Chlorhexidine	**Soap**	**Total**
Positive	20	18	38
Negative	6	10	16
Total	**26**	**28**	**54**
The two-sided P value is 0.3791, considered not significant. There is not a significant association between rows and columns. Odds Ratio = 1.852 95% Confidence Interval; 0.5600 to 6.124 (using the approximation of Woolf)			

3.7.1. Comparison between chlorhexidine and soap solution

'Chi – Square' Test			
	Triclosan	**Soap**	**Total**
Positive	17	18	35
Negative	10	10	20
Total	**27**	**28**	**55**

Chi – square statistic (with Yates correction) = 0.01039 with 1 degree of freedom. The two - sided P Value is 0.9188 considered not significant. There is not a significant association between rows and columns.

Odds Ratio = 1.059

95% Confidence Interval; 0.3527 to 3.178

(using the approximation of Woolf)

Fisher Exact Test			
	Triclosan	**Soap**	**Total**
Positive	17	18	35
Negative	10	10	20
Total	**27**	**28**	**55**

The two-sided P value is 1.0000 considered not significant. There is not a significant association between rows and columns.

Odds Ratio = 1.059

95% Confidence Interval; 0.3527 to 3.178 (using the approximation of Woolf)

3.7.2. Comparison between triclosan and soap solution

'Chi – Square' Test			
	Triclosan	**Chlorhexidine**	**Total**
Positive	17	20	37
Negative	10	6	16
Total	**27**	**26**	**53**
Chi - square statistic (with Yates correction) = 0.6520 with 1 degree of freedom. The two - sided P Value is 0.4194, considered not significant. There is not a significant association between rows and columns. Odds Ratio = 1.961. 95% Confidence Interval; 0.5898 to 6.519 (using the approximation of Woolf)			
Fisher Exact Test			
	Triclsoan	**Chlorhexidine**	**Total**
Positive	17	20	37
Negative	10	6	16
Total	**27**	**26**	**53**
The two-sided P value is 0.3718, considered not significant. There is not a significant association between rows and columns. Odds Ratio = 1.961 95% Confidence Interval; 0.5898 to 6.519 (using the approximation of Woolf)			

3.7.3. Comparison between triclosan and chlorhexidine

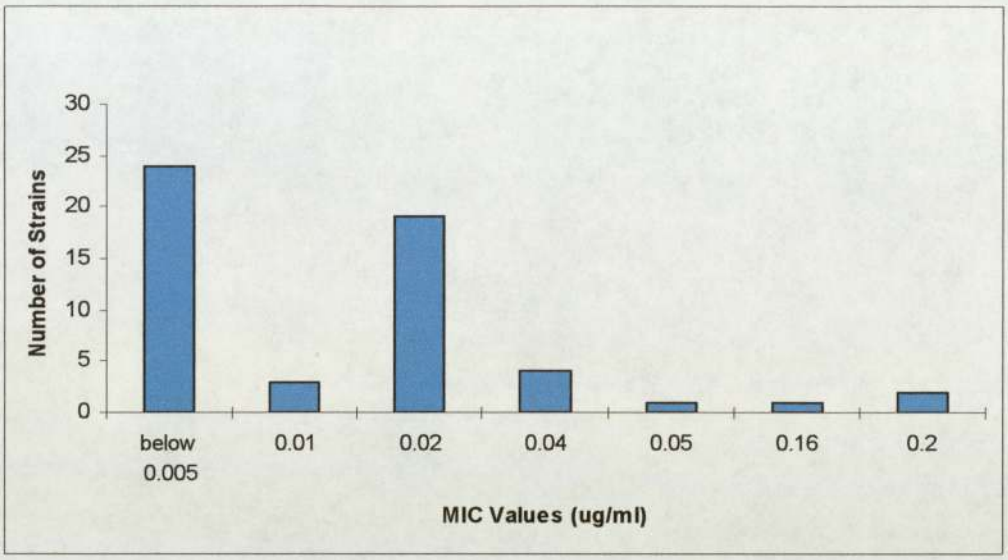
3.8. Minimum Inhibitory Concentration Results (MIC)

MIC Values in µg/mL			
Code	**Chlorhexidine**	**Triclosan**	**Soap**
1	0.4	0.05	> 16
2	< 0.005	< 0.005	2
3	0.04	< 0.005	> 16
4	0.5	< 0.005	> 16
5	0.5	0.01	> 16
6	0.5	0.01	0.4
7	0.5	0.02	0.1
8	0.4	0.02	0.2
9	< 0.005	< 0.005	2
10	0.2	< 0.005	0.1
11	< 0.005	< 0.005	2
12	0.5	< 0.005	1
13	0.4	0.02	0.4
14	0.5	0.02	0.4
15	0.4	0.02	> 16
16	0.4	0.02	> 16
17	0.05	< 0.005	0.4
18	0.05	0.2	> 16
19	0.5	0.02	> 16
20	0.5	0.04	0.1
21	0.5	0.02	0.1
22	0.5	0.02	0.1
23	0.5	0.04	> 16
24	< 0.005	< 0.005	2
25	< 0.005	< 0.005	> 16
26	0.5	< 0.005	0.2
27	0.5	0.02	> 16
28	0.4	0.02	> 16
29	< 0.005	< 0.005	2
30	0.2	0.16	> 16
31	0.5	0.02	0.16
32	0.5	< 0.005	> 16
33	0.4	0.02	> 16
34	0.2	0.2	0.1
35	1	0.02	0.1
36	0.4	< 0.005	0.1
37	0.2	0.02	0.2

MIC Values in µg/mL			
Code	**Chlorhexidine**	**Triclosan**	**Soap**
38	0.5	0.02	0.16
39	0.5	0.02	2
40	0.5	0.02	0.2
41	< 0.005	< 0.005	2
42	< 0.005	< 0.005	2
43	0.2	< 0.005	0.4
44	< 0.005	< 0.005	2
45	< 0.005	< 0.005	2
46	0.4	0.04	2
47	0.4	0.02	> 16
48	0.4	0.04	0.2
49	0.2	0.01	> 16
50	< 0.005	< 0.005	> 16
51	< 0.005	< 0.005	2
52	0.4	< 0.005	> 16
53	< 0.005	< 0.005	> 16
54	< 0.005	< 0.005	2

3.8.1. Comparison of MIC values for MRSA strains tested against three agents used

3.8.2. Triclosan



3.8.2. Chart to illustrate the MIC values of triclosan

Of the 54 strains tested against Triclosan:

44.4% of strains had MIC Values of < 0.005 μg/ml

5.5% of strains had MIC Values of 0.01 μg/ml

35% of strains had MIC Values of 0.02 μg/ml

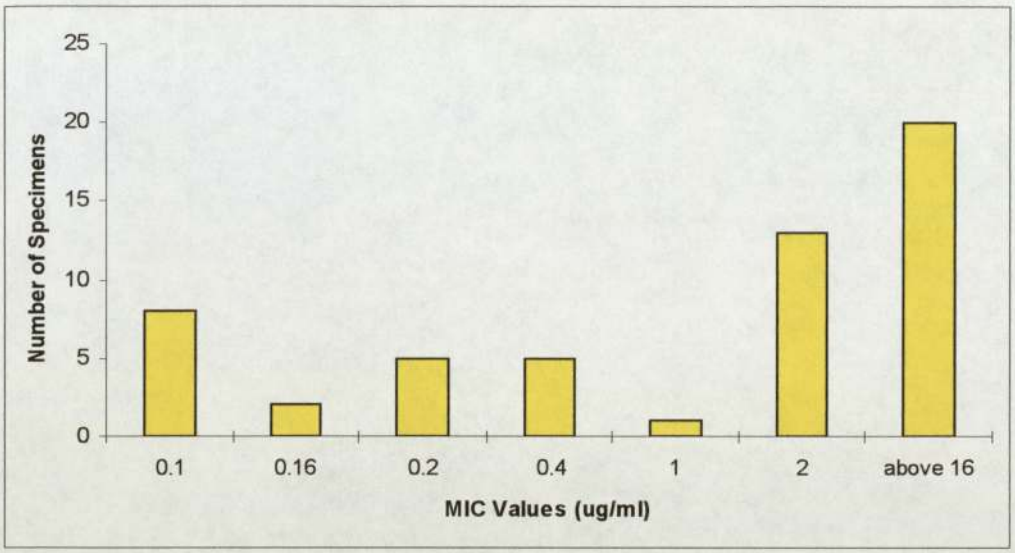
4% of strains had MIC Values of 0.04 μg/ml

1% of strains had MIC Values of 0.05 μg/ml

1% of strains had MIC Values of 0.16 μg/ml

2% of strains had MIC Values of 0.2 μg/ml

3.8.3. Soap



3.8.3. Chart to illustrate the MIC values of soap

Of the 54 strains tested against Soap:

14.8% of strains had MIC Values of 0.1 μg/ml

3.7% of strains had MIC Values of 0.16 μg/ml

9.2% of strains had MIC Values of 0.2 μg/ml

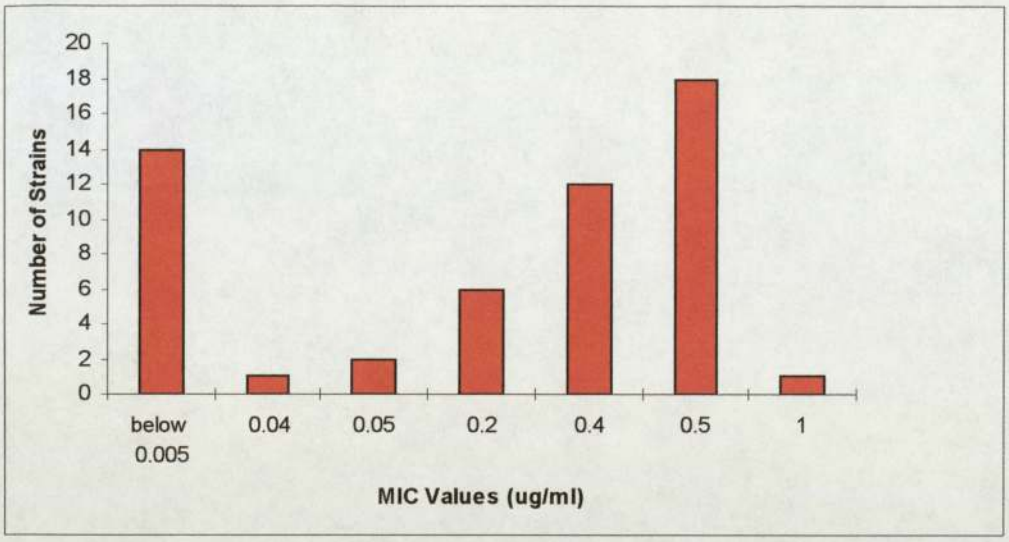
9.2% of strains had MIC Values of 0.4 μg/ml

1.8% of strains had MIC Values of 1 μg/ml

24% of strains had MIC Values of 2 μg/ml

37% of strains had MIC Values of >16 μg/ml

3.8.4. Chlorhexidine



3.8.4. Chart to illustrate the MIC values of chlorhexidine

Of the 54 strains tested against chlorhexidine:

25.9% of strains had MIC Values of < 0.005 μg/ml

1.8% of strains had MIC Values of 0.04 μg/ml

3.7% of strains had MIC Values of 0.05 μg/ml

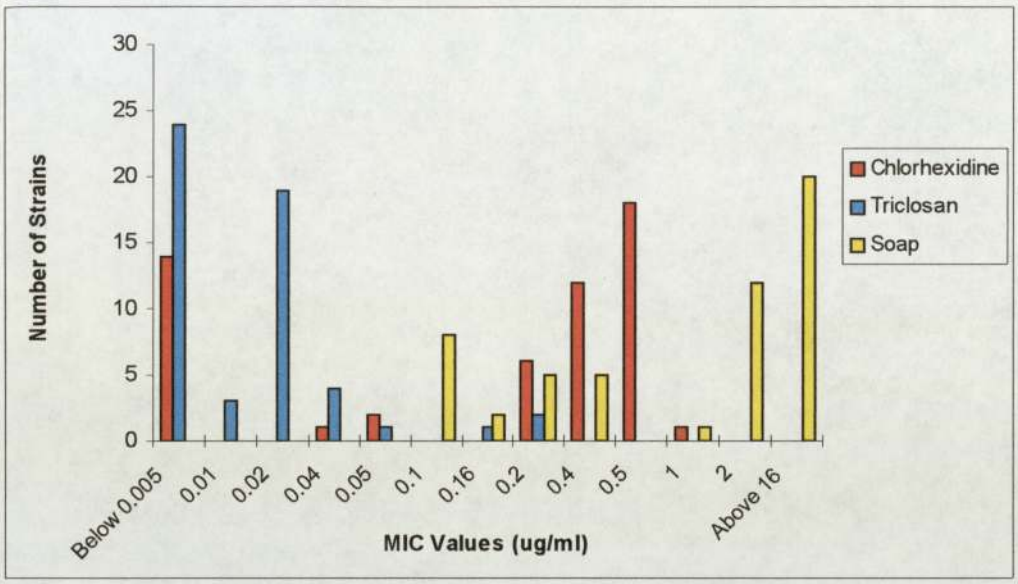
11.1% of strains had MIC Values of 0.2 μg/ml

22.2% of strains had MIC Values of 0.4 μg/ml

33.3% of strains had MIC Values of 0.5 μg/ml

1.8% of strains had MIC Values of 1 μg/ml

3.8.5. Comparison of the three agents used.

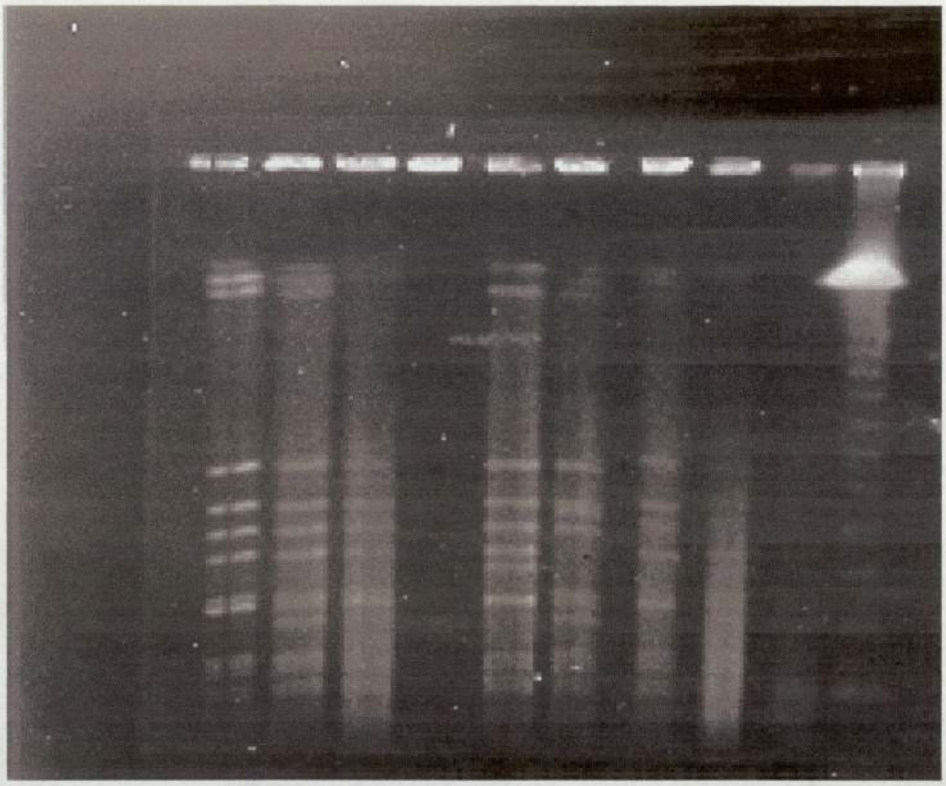


3.8.5. Graph to illustrate a comparison between MIC values of MRSA strains tested against chlorhexidine, triclosan and soap

To determine the antibacterial activity of the three agents used, MIC testing was undertaken. Of the 81 patients entered in the study, strains from 54 patients were tested. Of these, 27 strains were not available for testing either due to strains dying or not kept for sloping initially.

It can be seen from the above table (3.8.1.) charts (3.8.2-3.8.5.) that triclosan demonstrates greater anti-microbial activity towards the MRSA strains than chlorhexidine, which in turn has more activity than soap.

3.9. PFGE



3.9.1. MRSA strains typed by PFGE using Sma1 digestion of the chromosomal DNA.

Lane 1, strain 35; lane 2, strain 29; lane 3, strain 49; lane 4, strain 48; lane 5, strain 34; lane 5, strain 18; lane 7, strain 7; lane 8, strain 25; lane 9, stain 27; lane 10, lambda concatamer molecular weight markers.

It can be observed from the above picture that of the strains investigated, 7 gave patterns which could be interpreted. Of these, 4 were closely related, differing in 1 or 2 bands only. 2 of the strain differ from this group by more than 3 bands and the other appeared unrelated.

3.10. Comparison between antibiograms, MIC values, phage type and PFGE.

PFGE Lane (fig 3.9.1.)	Spec. Number	Anti-biogram	MIC Values (µg/ml)			Phage Type	PFGE
			Tric.	Chlor.	Soap		
1	35	P.M.	0.02	1	0.1	EMRSA 15	Closely related
2	29	P.M.	<0.005	<0.005	2	EMRSA 15	Closely related
3	49	P.M.	0.01	0.02	>16	EMRSA 15	Closely related
4	48	P.M.	0.4	0.04	0.2	Possible E15 Variant *	No result
5	34	P.M.	0.02	0.02	0.01	EMRSA 15	Closely related
6	18	P.M.	0.2	0.05	>16	N.T	Unrelated
7	7	P.M.	0.2	0.5	0.1	EMRSA 15	Unrelated
8	25	P.M.	<0.005	<0.005	>16	EMRSA 15	Unrelated
9	27	P.M.	0.02	0.05	>16	N.T	No result

3.10.1. Table to illustrate a correlation between antibiogram, MIC values, phage type and PFGE

key:- N. T. = Non typable
P = Penicillin
M = Methicillin

It can be seen from the above table that of the MRSA strains tested, they all had the same antibiogram. However, there were no common factors between the MIC values, phage type or PFGE results. It can be assumed that the strain identified as a 'possible EMRSA 15 variant ' is an EMRSA 15 since had the same antibiogram as strains 29, 34, 35 and 49.

4. DISCUSSION

The original study proposal was to review the effectiveness of two antibacterial agents when compared to soap, following one course of body washes and review the number of continuous courses required to achieve three negative MRSA screens. Due to problems occurring in the recruitment of patients into the trial, it was not possible to achieve either the expected sample size of 150 patients, or assess how many continuous courses were required to achieve three negative MRSA screens. These problems were attributed to the following factors:

- patient care pathways meant that patient length of stay in hospital is now shorter
- long stay patients were either too ill or too confused to consent.
- patients did not want to enter the trial due to the stigma associated with both MRSA and being in a trial.

Due to the above problems the researcher decided to evaluate only those patients who had received one course of body washes.

Whilst the final sample size of 81 patients was too small to give soundly-based statistical data, the researcher attempted to estimate the population size required to obtain statistically significant data, using both chi-square and Fisher-exact tests. To obtain statistically significant data

between chlorhexidine and triclosan it was estimated that the study group would have needed to have been increased four fold and the chlorhexidine and soap groups by six fold. However, because the numbers in the triclosan and soap groups were comparable, data would not have been statistically significant even after increasing the group size by six fold.

Whilst the results of the study did not reach statistical significance, they serve to demonstrate that a much larger study group would be required to obtain statistically significant data. Therefore, any further research would need to be both multi-centred and should include integrated hospital and community care to ensure recruitment from a broader section of the population.

Whilst the researcher appreciates that the numbers of patients entered into the study were too small to reach statistical significance both descriptive analysis and microbiological studies raised several issues for discussion.

Of the 81 patients entered into the study, 26 (32%) commenced on chlorhexidine, 27 (33%) commenced on triclosan and 28 (35%) commenced on soap. This was as a direct result of the randomised of

trial subjects to one of the three variables used as opposed to the selective allocation of agents.

The age distribution of patients' entered into the study demonstrates that whilst MRSA has the ability to colonise all age groups, it was more prevalent in the elderly population. However, it could be argued that the elderly are predisposed to acquiring MRSA due to chronic illness and frequent hospital admissions and therefore, the greater potential for the elderly to become colonised with MRSA should be expected. Because this study was hospital based any further research should be extended into the community to incorporate all age groups, ensuring an equitable assessment of the age distribution of patients with MRSA.

From the evidence presented it was clear that the elderly were not only dispersed across speciality groups but accounted for a higher proportion of patients being admitted to hospital. This was demonstrated by the high numbers of patients over 65 years who were entered into the trial. Therefore, infection control programmes need to consider the potential for elderly patients to be readmitted to high risk areas such as orthopaedics and vascular surgery, where the potential for clinical infections as opposed to colonisation is increased if structured infection control programmes are not in place.

Given the increased numbers of patients with MRSA, future investigations should consider previous studies by Garibaldi *et al.* (1985), Haley *et al.* (1985) and Bibby *et al.* (1986) which highlighted such factors as age and the number of hospital admissions as increasing the potential for patients to acquire an infection. Equally, because the NHS advocates integrated hospital and Community care, patients are often dispersed across disciplines and are cared for as part of a multi-disciplinary team. This means that the potential for patients to become colonised with multi-resistant organisms such as MRSA may be increased, both from patients being in different health care settings, and care being delivered by different health care personnel. Also, the elderly and patients with chronic medical problems not only have frequent hospital admissions but may also mix in the same circles through support groups. Cohort groups not only offer the potential to increase the risk of transmission of organisms such as MRSA but, reduce the likelihood of maintaining negative MRSA screens, as there is a perceived risk for patients to become recolonised in the presence of an increased environmental load. Therefore any future research should consider other possible vectors of transmission such as: links between specific groups i.e. hospitals; nursing and residential homes; day care centres; and the potential for some groups to become colonised with MRSA i.e. those with chronic illness such as diabetes or sickle cell disease.

The presence of a higher number of patients included in the trial being located in the Medical Directorate was a result of patients being randomised throughout the Trust as opposed to being selected by speciality groups. The number of wards in the Medical Directorate (17) far exceeded that of surgery (6), orthopaedics (2), and elderly care (1). One would therefore expect a higher percentage of patients with MRSA to be identified from the medical directorate than from other specialities.

Other factors may contribute to the higher numbers of patients with MRSA in the medical directorate as opposed to the surgical directorate. Surgical patients often remain in hospital for a shorter time. This is as a result of a number of factors:

- they are younger and generally fitter
- more operations are being performed as day cases
- surgical patients do not return for frequent re-admissions
- often they do not belong to support groups, or day centres.

Therefore, their potential to become colonised with MRSA is reduced as a result of less contact with potentially positive MRSA patients.

Data obtained from the information department within the Trust undertaking the study demonstrated the mean length of stay for surgical patients was 3 days, which is less than both the Medical Directorate (4 days), orthopaedics (5 days) and elderly care (19 days). The correlation between a marginal difference in the 'mean' length of stay for medical, surgical and orthopaedic patients and the potential for medical patients to become colonised and/or re-colonised with MRSA, may be as a result of:

- frequent hospital admissions
- links with support groups
- chronic medical conditions, which may predispose patients to poorer general health. This may have an influence on their immunity and susceptibility to acquire MRSA.

There are other points of consideration for the higher numbers of patients identified on the elderly care and medical wards with MRSA. Firstly, the effects of an increased environmental load of organisms in relation to the length of stay on patients becoming colonised while in hospital (especially if the patient has chronic lesions present). Secondly, the environment in which dressing changes are conducted varies from medical to surgical wards. Generally surgical wounds are initially dressed in theatre where the environmental load or organisms is greatly reduced as a result of filtered positive pressure airflow ventilation. This is opposed to patients on medical wards where, although dressings are done aseptically, the

potential environmental load is greater due to both the increased numbers of patients admitted who have MRSA, and the lack of mechanical room ventilation. Also surgical patients have dressing changes performed on the ward, but in the main the exposed surface area is small with minimal broken skin exposed. By contrast, patients on medical wards with chronic lesions such as leg ulcers, or pressure sores often a have larger surface area of broken skin.

The number of patients commenced on antibiotic therapy was too small to conclude any statistical significance. However, of the patients who received antibiotic therapy, there were insufficient data to draw any statistical conclusion. Of those patients who received vancomycin therapy, and had wound infections, the presence of a negative follow up screen from the 3 of the 5 patients would support the use vancomycin therapy for the treatment of systemic or clinical infections. However, 2 of the patients remained positive on lesion, nose and groin swabs, despite vancomycin therapy on follow up screening. This would contradict the theory that ongoing microbiological screening should not be undertaken during vancomycin therapy since it may result in a false negative. Unfortunately the numbers in this study are too small to conclude any statistical significance of the effects of vancomycin therapy. A larger study would be required to assess the effectiveness of vancomycin and other antibiotics (such as cephalosporins) on the level of skin colonisation. Any

further study should consider previous work by Brady *et al.* (1990) which highlighted the need to rationalise antibiotic prescribing and treatment as it could be influential in the controlling of an MRSA outbreak, and should be used as a control measure. The work of Brady *et al.* is supported in the report by SMAC – 'Path of least resistance' which addresses the use of antibiotics in the control and prevention of multi-resistant organisms.

This study did not include care in the community and assess the acquisition rate of community acquired MRSA. However, from the data collected, the presence of a high number of patients identified as nasal carriers suggests that a proportion of those admitted to hospital have either:

- acquired MRSA in the community
- had frequent hospital appointments
- re-admissions as a result of underlying medical conditions
- or patients were part of a specific cohort e.g. elderly attend similar functions predisposing themselves to become colonised with MRSA.

The presence of a number of patients being identified as MRSA positive on admission suggests MRSA was community acquired. However, research undertaken by Fraise *et al.* (1997) evaluating the prevalence of MRSA in nursing homes suggests that while there was a high prevalence

of MRSA in the community, the MRSA strains potentially originated in hospital.

The presence of patients found to be positive on follow up screens could be as a result of no initial isolate being sent. Therefore it could be argued that the organism was present but not detected, or their initial screen was negative but the presence of the organism from another site resulted in transmission either endogenously or exogenously (in the environment in which they were nursed) resulting in the patients becoming re-colonised. These conclusions support the theory suggested by Ayliffe *et al.* (1992) on transmission of organisms and the studies of Ward *et al.* (1981), Winn *et al.* (1980), and Yu *et al.* (1980) on nasal carriage becoming re-colonised over time.

Owing to the time scale the researcher was unable to perform PFGE on all MRSA stains. Nine MRSA strains were randomly selected but only 7 of these could be analysed. The common pattern obtained for four of the strains possibly indicated the existence of a common hospital stain, which would support previous work by Fraise *et al.* (1997). Although PFGE can offer a reliable method of distinguishing MRSA strains for routine analysis is both costly and time consuming and would be impractical for routine clinical use.

Whilst the number of strains reviewed by phage typing was limited due to time restrictions EMRSA 15 was found to be a predominant strain. EMRSA 15, has long been recognised as the prevalent UK epidemic strain and has been responsible for the high incidence of MRSA in many hospitals over recent years. These findings would support both the work identified in this study and that of Fraise *et al.* (1997) which suggests that those strains identified in the community, originated in hospitals. Of the strains tested there was no correlation between the MIC values, antibiogram and the agents used.

Recent guidelines advocate the use of mupirocin to reduce nasal carriage (Duckworth, 1990; Ayliffe *et al* 1998). Evidence from this trial would suggest that of those patients found to have nasal carriage of MRSA, the use of mupirocin had little effect, supporting earlier works by Ward *et al.* (1981); Winn *et al.* (1980) and Yu *et al.* (1986). It could therefore be argued that the use of antibiotics in a non outbreak situation should be used with caution to prevent encouraging resistance, which could potentially reduce a patient's antibiotic therapeutic options if antibiotic therapy is required at a later date to treat a clinical infection (Smith *et al.* (1987); Rahman *et al.* (1988); Cookson, (1990); Cookson, (1998); Ambler & Drabu, (1996); DOH (1998); Smith and Kennedy, (1998)). However, as with body washes, when reviewing the effectiveness of mupirocin,

consideration needs to be given to both its application and compliance by the patient to use it as prescribed. However, because the numbers entered into the study were too small to be statistically significant a further period of study is required to assess the long-term use of mupirocin and the incidence of nasal recolonisation.

A review of the numbers of patients negative for MRSA following one course of body washes demonstrated triclosan (58%), and soap (55%) to be better than chlorhexidine (30%). The overall numbers were too small to demonstrate any statistical significance between the 3 agents used. These initial findings were similar to those of Faogalis *et al's.* (1995) who found no statistical baseline difference following a single application. The presence of no baseline difference between chlorhexidine, triclosan and soap may be attributed to the presence of bronopol as a preservative, exerting antimicrobial activity. Therefore, any future works to review the reduction of MRSA skin colonisation should consider the effectiveness of any preservative which may be present in soap.

A review of the MIC values showed triclosan to exert better antibacterial activity than chlorhexidine, which in turn was better than soap supporting previous work by Simpson *et al.* (1994) who concluded that antibacterials are superior to soap. However, when reviewing the literature, no one agent is shown to be consistently better. Ayliffe *et al.* (1988) found

chlorhexidine to be better while Huang *et al.* (1994) found chlorhexidine to have a marginal effect over soap. Therefore in the clinical setting a major factor of the effectiveness of a body wash is not the named agent used but rather the application of the agent, supporting work by Bamber and Neal (1999). Equally when comparing studies which have been undertaken to look at antibacterials as hand disinfectants the technique of applying the solution is as important as the solution itself.

This is particularly relevant when applying body washes as this study indicated that a proportion of patients either remained positive for MRSA in their groin and/or on their fingers, or were subsequently found positive for MRSA on follow up screens. This could be considered to be as a result of the agents used being ineffective in reducing the level of skin colonisation of MRSA, or the manner in which the solution was applied was inadequate and not consistently applied to all areas of the body in a standardised manner. Other factors which may influence the application and effectiveness of the agents used were patient weight, since excess skin folds may increase the likelihood of areas of the body not being washed in a standard manner as previously described.

Another issue for consideration is whether MRSA can be transiently carried. It cannot be assumed from one negative screen that a patient's level of skin colonisation has been permanently eradicated, it may be

temporarily reduced to a low level, which is not detected by the screening method used.

When considering the effectiveness of antibacterials thought needs to be given to the residual and accumulative affect of the agents used. Publications by Bhagaava and Leonard (1990) and Ciba-Geisy Corp (1995) highlight the residual effects of triclosan, whilst work by Ayliffe *et al.* (1988) highlights the residual effect of chlorhexidine. Because this study only reviewed the effectiveness following one course of body washes consideration needs to be given to previous work as described above and that of the Faogalis *et al.* (1995) who also concluded antibacterials had a better cumulative affect. Future work is required to look at the duration of treatment required to produce any significant benefit when looking at the effects of long-term use. Consideration should be given to recruitment of sufficient numbers into the trial, the practicalities of achieving consistent application of the agents and the potential for sensitisation and irritation of the skin with protected use. Equally, given the fact that patients remain in hospital for shorter lengths of stay, any further studies should be multi-centered and include the community.

When evaluating body washes for use in the clinical environment, consideration should be given to the general condition of patient's

undergoing treatment. Work by Russell and Day (1993) identified the influence that the pH and the presence of organic matter have on antibacterials, in particular chlorhexidine. It could therefore be argued that the presence of chronic lesions such as leg ulcers could reduce the effectiveness of antibacterials used, if a large amount of organic matter were present on the surface of the skin.

Of the patients identified in this study as having lesions, there was little difference between the growth of organisms pre and post washing with one of the designated agents. This may be as a result of either the lesions being covered with a designated dressing and not washed with one of the chosen agents, therefore reducing the potential for the agents to work, or contamination from another positive body sites has prevented reduction in the organism load. This latter theory may support the presence of sites identified as positive with MSSA being identified as MRSA on follow up screens.

Other areas for consideration are the effect that the pH of a patient's skin has on the ability for MRSA to survive and the ability for patients to remain colonised with MRSA. Equally, future work should also consider any correlation between groups more prone to become colonised with MRSA e.g. elderly and those patients with chronic medical conditions.

In today's health care climate patients are more aware of both their clinical condition and channels for complaint in the event of dissatisfaction. As in the USA, UK patients are increasingly following legal channels as a form of redress for hospital acquired infections. Therefore the continued search for an effective method of eradication or reduction of MRSA colonisation is a worthwhile aim. Not only in treating the individual, but to reduce the potential for environmental contamination, and therefore lowering the risk of cross infection of multi-resistant organisms to others in the same setting.

5. CONCLUSION

In conclusion, whilst the overall numbers were too small for the results to achieve statistical significance, this research project has served to demonstrate that in the clinical environment there is little difference between triclosan, chlorhexidine or soap. However MIC testing demonstrated that triclosan was more active than chlorhexidine, which in turn was more active than soap against MRSA. This would suggest that when selecting a body-wash the effectiveness of the agent used is influenced by its application. Therefore, a conclusion that can be drawn from this study is that, anti-bacterial body washes are no more effective than soap alone. Furthermore, the potential development of resistance to triclosan and chlorhexidine could be avoided if soap was used alone. Also from a review of the literature and the evidence presented in this study the use of topical mupirocin to eradicate nasal carriage of MRSA has little effect. Therefore, given the potential for antibiotic resistance, the need for routine use of nasal mupirocin in the treatment of patients colonised with MRSA should be used with caution.

From the evidence presented in this study, and a review of the literature, infection control programmes aimed at reducing MRSA skin colonisation should consider:

- the residual effects of antibacterials in relation to the patients' length of stay, giving consideration to the use of antibacterials for 'short stay' patients
- the patient's clinical condition and the environment in which they are nursed.

A recent Government initiative aimed at providing a cost effective quality led service means that Trusts have to utilise resources effectively. Given the numbers of MRSA patients cared for in the NHS today the use of antibacterials has increased the pharmaceutical budgets of many Trusts and therefore consideration should be given to streamlining their use both as a means of preventing resistance in the long term, and to reduce costs.

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APPENDIX 1

WARD STAFF INFORMATION SHEET

'How effective are anti - bacterial skin disinfectants in the eradication/ reduction of Methicillin Resistant *Staphylococcus aureus* (MRSA) skin colonisation.'

RESEARCH METHODOLOGY

1. PATIENTS CRITERIA FOR ADMISSION TO STUDY

(i) All patient's identified as positive for MRSA from Microbiological sampling from any site from specimens obtained either from Clinical samples or admission screens.
(ii) Ensure all patients understood and signed the consent form.

2. EXCLUSIONS TO STUDY

(i) Patients with known skin conditions.
(ii) Patients found to have had topical treatment (e.g Mupirocin or Aquasept/ Hydrex Washes) in the last two weeks .

3. WITHDRAWAL FROM STUDY

(i) Reaction to antibacterial agents used in the study.
(ii) Patient's no longer wish to participate in the study.

4. ALLOCATION OF AGENTS TO BE USED

A comparative randomised study of one of three different agents.
(i) Triclosan 2% (Aquasepts)
(ii) Chlorhexidine 4 % (Hydrex)
(iii) Non medicated soap (Deb)

NB Where nasal carriage of MRSA is identified Mupirocin Nasal cream will be used twice daily for 5 days as per existing hospital protocol.

5. APPLICATION OF AGENTS

Following wetting of the skin with water 10 mls of the allocated agent will be applied using a wipe to the whole body surface avoiding the eyes. Hands should be washed with the antibacterial agent/ soap,.followed by a conditioner if routinely used by the patient.

6. DURATION OF TREATMENT

Treatment e.g antibacterial agent or soap will be used for a total of 5 days, Mupirocin will be used nasally if MRSA is found on nose swabs. Both the anti bacterial agent and Mupirocin, if used will be stopped for 48hrs and the patient rescreened as per protocol.

7. TREATMENT FORM

Upon identification of a patient found to be positive for MRSA a treatment sheet will be allocated. Please complete the sheet, inserting the date of treatment. These will be collected by the CNSIC. Any comments i.e application/ reaction to agents should be written on the form, noting the patients skin condition before and after treatment.

Any queries or concern please contact either Rebecca Evans or Kathy Mitchell - Infection Control on Bleeps 1707 or 1169.

Please ensure that any patient included in the study has signed a consent form.

Thanking you for your help and co - operation

Rebecca Evans
Clinical Nurse Specialist
Infection Control

CITY HOSPITAL NHS TRUST
DUDLEY ROAD, BIRMINGHAM. B18 7QH
www.cityhospital.org.UK

INFECTION CONTROL TEAM
TEL: (0121) 554 3801 FAX: (0121) 507 4448

CLINICAL NURSE SPECIALISTS INFECTION CONTROL

	BLEEP	EXT
Rebecca Evans B.Sc(Hons) RGN, RM	1707	4982
Carlton Murdock RGN	1232	5193/4
Yvonne Pritchard RGN	1169	5193/4

INFECTION CONTROL DOCTOR/ CONSULTANT MICROBIOLOGISTS:

	EXT
Professor R Wise MD,FRCP,FRCPath.	4255
Dr A Fraise MB,BS,FRCPath	4825
Dr M Gill B.Sc,MB,.ChB,MRCPath	5526
Dr T Weller MD,MRCPath	5742

MRSA TREATMENT SHEET

PLEASE COMPLETE AND RETURN TO CNS-INFECTION CONTROL. ARDEN HOUSE.

NAME.....UNIT NO.....WARD.....CONS.....
has been found to be positive for MRSA on screening on.....

RESULTS:-

It is advised that he/she is commenced on:-

1. **Daily baths/bed baths with Triclosan for 5 days.***

   If the skin becomes dry or shows signs of irritation, discontinue use and inform both Clinicians and Clinical Nurse Specialists Infection Control.

2. **Application of Mupirocin nasal cream to both nostrils twice daily for 5 days.***

- **Delete as appropriate.**

We will continue to monitor the patient's MRSA status throughout his/her admission and his/her notes will be labelled to enable us to follow him/her through subsequent admissions.

To ensure we are able to monitor the patient's progress please complete the following information.

1. **Condition of skin prior to washes;-**

2. **Date Triclosan body washes commenced.....**

3. **Date Triclosan body washes finish.....**

4. **Please insert date into top box and tick bottom box on completion of each wash.**

T	T	T	T	T	S	S

A = AQUASEPT (TRICLOSAN)

5. **Condition of skin on completion of course of washing.**

6. **Rescreen date.....**

7. **Rescreen results.**

Site	Organism	Resistancy
Nose		
Buttocks		
Fingers		
Groin		
Lesion 1		
Lesion 2		
Lesion 3		
Lesion 4		
CSU		
Sputum		

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MRSA TREATMENT SHEET

PLEASE COMPLETE AND RETURN TO CNS-INFECTION CONTROL. ARDEN HOUSE.

NAME.....UNIT NO.....WARD.....CONS.....
has been found to be positive for MRSA on screening on.....

RESULTS:-

It is advised that he/she is commenced on:-

1. **Daily baths/bed baths with Chlorhexidine for 5 days***

   If the skin becomes dry or shows signs of irritation, discontinue use and inform both Clinicians and Clinical Nurse Specialists Infection Control.

2. **Application of Mupirocin nasal cream to both nostrils twice daily for 5 days.***
   - **Delete as appropriate.**

We will continue to monitor the patient's MRSA status throughout his/her admission and his/her notes will be labelled to enable us to follow him/her through subsequent admissions.

To ensure we are able to monitor the patient's progress please complete the following information.

1. **Condition of skin prior to washes;-**

2. **Date Chlorhexidine body washes commenced.....**

3. **Date Chlorhexidine body washes finish.....**

4. **Please insert date into top box and tick bottom box on completion of each wash.**

C	C	C	C	C	S	S

H = HYDREX (CHLORHEXIDINE)

5. **Condition of skin on completion of course of washing.**

6. **Rescreen date.....**

7. **Rescreen results.**

Site	Organism	Resistancy
Nose		
Buttocks		
Fingers		
Groin		
Lesion 1		
Lesion 2		
Lesion 3		
Lesion 4		
CSU		
Sputum		

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Dr T Weller MD,MRCPath	5742

MRSA TREATMENT SHEET

PLEASE COMPLETE AND RETURN TO CNS-INFECTION CONTROL. ARDEN HOUSE.

NAME.....UNIT NO.....WARD.....CONS.....
has been found to be positive for MRSA on screening on.....

RESULTS:-

It is advised that he/she is commenced on:-

1. **Daily baths/bed baths with soap for 5 days.***

   If the skin becomes dry or shows signs of irritation, discontinue use and inform both Clinicians and Clinical Nurse Specialists Infection Control.

2. **Application of Mupirocin nasal cream to both nostrils twice daily for 5 days.***

   *** Delete as appropriate.**

We will continue to monitor the patient's MRSA status throughout his/her admission and his/her notes will be labelled to enable us to follow him/her through subsequent admissions.

To ensure we are able to monitor the patient's progress please complete the following information.

1. **Condition of skin prior to washes;-**

2. **Date body washes commenced.....**

3. **Date body washes finish.....**

4. **Please insert date into top box and tick bottom box on completion of each wash.**

S	S	S	S	S	S	S

S = SOAP

5. **Condition of skin on completion of course of washing.**

6. **Rescreen date.....**

7. **Rescreen results.**

Site Nose	Organism	Resistancy
Buttocks		
Fingers		
Groin		
Lesion 1		
Lesion 2		
Lesion 3		
Lesion 4		
CSU		
Sputum		

APPENDIX 5

INFORMATION SHEET

Methicillin Resistant Staphylococcus aureus (MRSA) treatment - How effective is it?

My name is Rebecca Evans. I work as a Clinical Nurse Specialist in Infection Control (CNSIC).

MRSA is a germ which many people have on their skin and usually causes no problems. This germ has been found on your skin. You will be given an additional sheet which gives you more information about MRSA and what it means to you.

I would like to ask for your help in a study to find out the best way of getting rid of MRSA from the skin. If you agree to do this we will give you either a skin antiseptic (one of two) or a liquid soap to wash in every day and to apply an antibiotic cream to your nostrils if the germ has been found there. You will have regular swabs taken from your skin and nose to check your progress. At present we do not know which is the best way of getting rid of the germ, so to find out we will give you one of the treatments decided by chance (i.e neither you nor the nurse will decide which treatment to give).

You do not have to take part in this study and if you decide not to take part in the study, it will not affect any part of your clinical management/medical care.

You are free to withdraw from the study at any time, without giving a reason. Please ask the Infection Control specialist nurses if you have any queries, we are available by telephone on 554 3801 Bleep 1707 or 1169 or ask a member of the ward staff to contact us . 'If you have any concerns about this study and wish to contact someone independent, you may telephone 0121 507 4396'

Thank you for your time and co-operation.

If you agree to take part in the study please sign the consent form overleaf.

10 Can visitors to the ward catch MRSA?

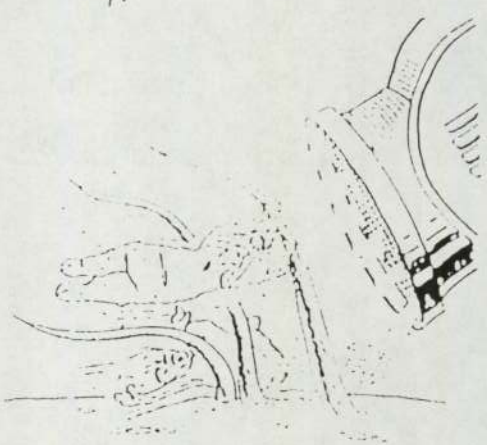
Healthy people are at very little risk of catching MRSA. They should keep cuts covered with a waterproof dressing and ensure they wash their hands thoroughly on leaving the ward. All visitors should see the nurse in charge before visiting. The nurse will give guidance and instruction on the prevention of spread of infection.

11 Can visitors infect other people?

Not if they wash and dry their hands before and after visiting.

12 Are there any special instructions or precautions on discharge from hospital?

If the patient still has MRSA a district nurse will visit and treat but the main precaution is to continue handwashing with soap and water and *thorough drying*. Special ointments or washes may continue to be prescribed for a while after discharge.



13 Will my marital and sexual life be affected?

No.

If you have any other questions or would like more information,

METHICILLIN-RESISTANT STAPHYLOCOCCUS AUREUS

(M.R.S.A.) PATIENT INFORMATION LEAFLET

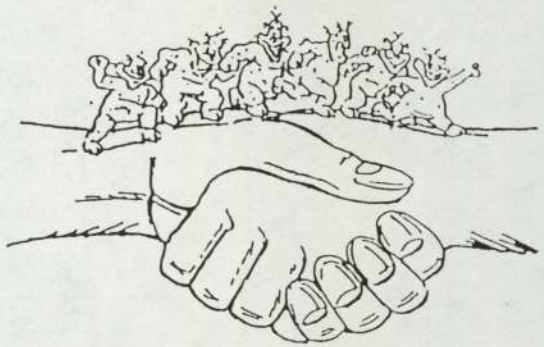
ROYAL COLLEGE OF NURSING

Appendix 6

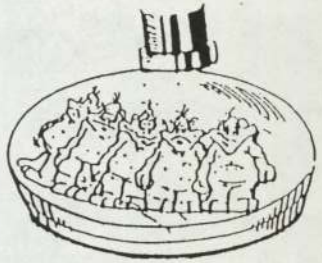
It is a bacterium which is not easily killed by the more commonly used antibiotics.

2 How does it affect me?
Nothing is visible but it may delay the healing process.

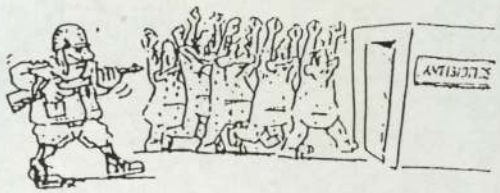
3 How did I catch MRSA?
It is one of the bacteria found in the environment from time to time and will do little or no harm unless it invades the body. The spread is usually by human contact.



4 How is MRSA identified?
By taking a specimen and sending it to the laboratory to be examined.

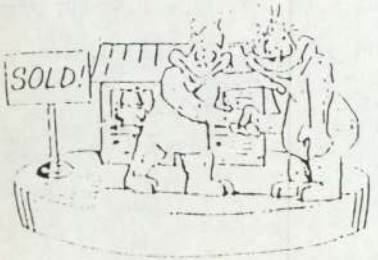


5 Can it be treated?
Yes, very successfully, by prescribed ointment, washes or antibiotics.

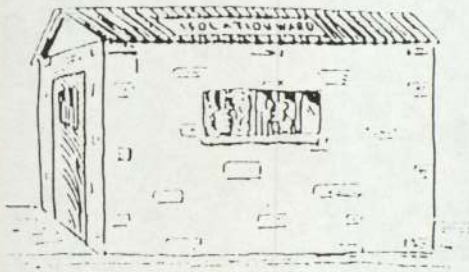


Only when repeated specimens show no growth of the bacterium.

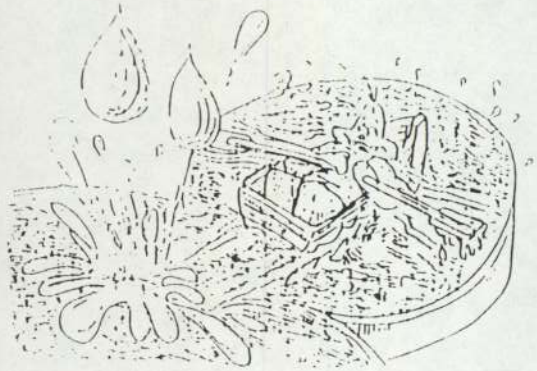
7 Can it come back?
Yes. Be careful with personal hygiene and handwashing. Be especially careful not to touch areas of broken skin and keep damaged skin covered.



8 Why are patients with MRSA nursed in an isolation ward or room?
To prevent the spread of the bacterium to other patients, who may be more vulnerable.



9 How can the spread of the MRSA be minimised?
By the thorough washing and drying of hands of everyone involved.



APPENDIX 7

How effective are anti-bacterial skin disinfectants in the eradication/reduction of Methicillin resistant staphylococcus aureus (MRSA) skin colonisation.

CONSENT FORM

NAME [BLOCK CAPITALS].....

UNIT NO:.....

I have read and understood the reasons for the study and agree to have specimens taken as necessary.

Signature:- .....

Witnessed:- .....

I have explained the purpose of the study and the procedure to the individual.

Name:- .....

Signature:- .....

Designation:- .....

Date:- .....

APPENDIX 8

INFECTION CONTROL: MRSA AUDIT

Unit No Pt name Cons *Please affix patient sticker*	Ward	1 2 3 4 5

Speciality: Elderly care ☐ Medical ☐ Surgical ☐ Orthopaedics ☐ Eye ☐

Skin Prep: Aquasept ☐ Hydrex ☐ Soap ☐

Procedure: ☐ Diagnosis ☐

Antibiotic usage

Vancomycin	Beta lactams	Cephlosporins	4 Quinolones	Other

Trial start Date____/____/____

Date of Rescreening	Positive	Negative	Comments

No of screens taken to obtain negative screen ☐

Other contributory factors not elsewhere classified