Recommendations for the Control of Methicillin-Resistant Staphylococcus aureus (MRSA)

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1. INTRODUCTION

Nosocomial infection is a major problem in the world today; 5-10% of all patients in hospital at any one time acquire such an infection, often caused by antibiotic-resistant organisms, with methicillin-resistant *Staphylococcus aureus* (MRSA) showing a particular ability to spread in hospitals, and now present in most countries. Methicillin-resistant *Staphylococcus aureus* strains are usually resistant to several antibiotics, in addition to the penicillinase-resistant penicillins and cephalosporins, and occasionally are sensitive only to vancomycin and teicoplanin. They vary in virulence, but are not usually more virulent than methicillin sensitive strains (MSSA). Epidemic spreads may occur; the definition of epidemic varies, but usually indicates spread in more than one ward in a hospital, or in more than one hospital, and the highly transmissible strains tend to spread to a number of hospitals. However, no laboratory test to determine virulence or transmissibility is available.

MRSA precipitates infections similar to those caused by sensitive strains of *S. aureus*, e.g. wound, lower respiratory and urinary tract infections, sepsicaemia, infection of sites involving invasive devices, of pressure sores, of burns, and of ulcers. Severe infections are more common in intensive care and other units with susceptible patients (e.g. burns and cardiothoracic units), but are uncommon in neonatal units, and colonisation without clinical infection is common in long-term care wards for the elderly. There is considerable variation in numbers of clinical infections among units, hospitals, countries, and among individual strains.

Some of the properties of MRSA and risk factors for infection are shown in Table 1. The spread of MRSA occurs from person to person, from either a colonised or infected patient, or a member of staff, the main route of spread being through the hands of staff. The inanimate environment is of lesser importance, but airborne spread is likely in the presence of heavy dispersers, e.g. in burns units. The incidence of colonisation or infection depends on the type of hospital, patient risk factors, transmissibility of the strain, rapidity of detection, and the speed and efficacy of control measures. Control efforts should be based initially on rapid identification of the organism, on elimination procedures, and on prevention of spread to other wards or hospitals. Rapid detection depends on accurate information concerning patients with an MRSA problem who are transferred from other hospitals, and on an efficient and reliable microbiological laboratory able to screen suspected patients for possible isolation. Handwashing/disinfection by staff after handling an infected or colonised patient, or his immediate surroundings, is a key preventive measure; avoiding transfer of patients or staff from an affected ward or unit to another ward or hospital is also vital.

A major problem is the detection of the organism when it first appears in a hospital. A good colonising strain can spread widely without being detected by the routine sampling of clinical infections. Colonisation sites can vary, e.g. nose, perineum, other areas of skin particularly if already damaged, and, less commonly, rectum or vagina. Sampling of only one or two sites may fail to detect the organism which the laboratory may take two or three days to identify. As special tests are needed to identify the organism, there should preferably be a microbiological laboratory in every large hospital where basic identification
tests can be carried out reliably. If this is not possible, a district laboratory could fulfil this role, provided communications and transport are good, and could also confirm results of antibiotic sensitivity tests, if necessary. A National Laboratory, or WHO Collaborating Centre, should be available to collect data on antibiotic resistance, to type strains if necessary, and to organise quality control procedures throughout the country. Their microbiologists or epidemiologists should also be available to provide advice and assistance to hospitals with an MRSA problem.

Preventive measures, particularly monitoring and typing, should be organised nationally, although simple guidelines, introduced at the local level, could be effective, if properly implemented. Medical staff and management in hospitals must be convinced that MRSA is a real problem and must be encouraged to provide their support to the preventive programme as the "global" problem may not be obvious to an individual clinician with a minimal clinical problem and with few infected MRSA patients.

The increasing resistance of MRSA and other organisms render it essential that these strains be detected and eradicated wherever possible. If the spread of resistance continues, many infections will again become untreatable in the future.

2. EMERGENCE AND INTERNATIONAL SPREAD

The introduction of methicillin in 1960\(^1\) was soon followed by reports of resistance. In London in 1961\(^2\), Jevons reported one resistant strain in 5000 isolates. Reports of other isolates followed\(^3\), including reports from Turkey\(^4\) and Poland\(^5\) even though methicillin or any other penicillinase-resistant penicillin were not yet used in these countries.

During the 1960s, increased numbers of strains and infections were reported, mainly from Europe. They were usually resistant to penicillin, tetracycline, erythromycin and neomycin in addition to methicillin, other penicillinase-resistant penicillins (e.g. oxacillin, cloxacillin), and cephalosporins\(^6\)\(^7\). In Zurich, the percentage of MRSA isolates increased from 9.7% in 1965 to 16.1% in 1967\(^8\). In the United Kingdom, isolates sent to the Central Public Health Laboratory increased from 3/5440 (0.06%) in 1960 to 293/7153 (4.1%) in 1969. Screening in eight London teaching hospitals showed that 8.0% of isolates were methicillin-resistant\(^9\). Resistant strains were common in Denmark (46% of hospital strains in 1971)\(^10\)\(^11\). In a Sydney hospital, isolates increased from 0.7% in 1965, to 5.7% in 1969 and to 18.5% by 1970\(^12\)\(^13\). An increase in resistant strains was also reported from France and from India\(^14\)\(^15\). The distribution of resistant strains varies where outbreaks predominate in large hospitals (69 infections were reported in a U.K. general hospital in 1965)\(^16\). Outbreaks have also been reported from Newcastle and Birmingham, U.K.\(^17\)\(^18\).

Although resistant strains had been isolated in the USA between 1960 and 1975, reports of outbreaks were rare\(^19\). At the same time, other workers were reporting a decrease in the number of multiple-resistant methicillin-sensitive strains in the USA\(^20\) and in England\(^21\). This reduction was thought to be due to the more rational use of antibiotics and improved infection control.
In the 1970s and early 1980s, MRSA decreased in Europe. In Zurich, the isolation rate fell from 20% in 1971 to 3% in 1975. In Denmark, the frequency of isolation rose to 15% between 1967 and 1971, but decreased to 0.2% in 1984 and has since remained at a very low level. In St Thomas' Hospital, London, methicillin resistance fell from 2% in 1973 to 0.5% in 1977. In a general hospital in Birmingham, U.K., methicillin-resistant strains fell from 8.5% in 1970 to less than 0.5% in 1977. Most of the infected or colonised patients were in surgical or orthopaedic wards. In the burns unit in Birmingham, U.K., MRSA were still frequently isolated in 1976, e.g. over 40% of isolates, but decreased to 0% in 1984. The reason for the reduction in the U.K. and in Scandinavia is unknown. A possible explanation is less use of tetracycline (and streptomycin) leading to the disappearance of certain strains, e.g. phage types 83A, 29/77 (see Table 2). These strains may initially have been highly transmissible but this property was subsequently lost. Another less likely explanation is that the introduction of gentamicin reduced the number of multiple-resistant gentamicin-sensitive strains; the new outbreak strains in the 1980s were often resistant to gentamicin. There was no evidence of an increase in the use of penicillinase-resistant penicillins during this period.

Another explanation is that the improved infection control and laboratory surveillance may have played a role. The introduction of an isolation unit in Newcastle, U.K. was associated with a reduction in MRSA over a 6 month period, but the role of the isolation unit is difficult to assess; the introduction of an isolation unit in Birmingham gave a similar result when the number of MRSA were already falling. Although there are no well controlled studies, isolation units were associated with control of outbreaks in the early days of staphylococcus outbreaks with epidemic methicillin-sensitive strains. However, the issue was complicated in the mid 1970s by the emergence of new strains of MRSA, often resistant to gentamicin, in the U.K., France, and some other countries; in the late 1970s, epidemics were reported in Ireland, Australia and the USA. In Dublin hospitals, 5.4% of strains were methicillin-resistant in 1971 and outbreaks have continued to occur. Methicillin-resistant S. aureus represented less than 2% of outbreaks in Australia before 1975, but by 1979, 31 hospitals were involved in outbreaks and, in six of these, 20-40% of isolates were resistant. Since then, 200-300 new cases have been reported in some hospitals each year. These included cases in neonates and in immunosuppressed patients, and infection of surgical wounds. Septicaemia was frequently reported in association with intravascular devices. A summary of antimicrobial resistance in 7500 isolates (1986) showed a percentage of 14.4% of MRSA on average for Western Australia, ranging from 25% to 0.4%.

Although MRSA continued to be isolated in the late 1970s in the U.K., large outbreaks were rare. The first of the new major epidemic strains appeared in London hospitals in 1981 where it caused severe infections, including septicaemia, endocarditis and meningitis. Since then over 1000 patients have been affected in one London hospital while the strain continued to cause major outbreaks in other London hospitals and elsewhere, particularly in southeast England. A number of other epidemic strains have emerged, tending to be concentrated in certain regions. By 1991, 14 epidemic strains had been described. Although control is possible in individual wards or hospitals, the spread has continued. Two new strains appeared in the east and west Midlands in the 1990s.
and have gradually spread to other hospitals, whereas the original southeast England strains (known as EMRSA 1 and 2) have decreased. A new strain emerged in the Birmingham, U.K., burns unit after several years' absence of any MRSA, but rarely caused clinical infection (personal observation). The overall picture in the U.K. is one of a low incidence of sporadic strains before 1981, followed by the emergence of various epidemic strains thereafter.

Major outbreaks have been rare in Denmark, Sweden, and the Netherlands, although strains have been imported from other countries. Rosdahl attributes the lack of spread in Denmark to early, reliable detection, good antibiotic control, and immediate implementation of control procedures when an MRSA strain is imported. Similar reasons have been proposed for the Netherlands. Nevertheless, many hospitals with good control procedures have failed to limit spread of epidemic strains.

Few MRSA were isolated in the USA in the early and mid-1960s, a time when there were major problems in Europe, the first large outbreak being reported in 1968 and followed shortly after by others. A survey of hospitals between 1975 and 1980 indicated that MRSA was present in 145 hospitals in 36 states, particularly in hospitals with over 30 beds. In one of the early outbreaks, 201 patients were colonised or infected, of which 156 were in a burns unit. A review of outbreaks in 1982 showed that none was associated with operating theatres, whereas 12 out of 18 involved critical care units (e.g. burns). Other studies have confirmed the extent of MRSA, mainly in large U.S. hospitals.

A later review in 1987-1989 showed similar results. Isolates collected in the National Nosocomial Infections Surveillance Study showed an increase in methicillin-resistance from 2.4% in 1975 to 29% in 1991, irrespective of the size of the hospital. Long-stay hospitals for care of chronically ill patients can also be reservoirs for MRSA, and transfer of infected or colonised patients back to an acute hospital can initiate a new outbreak. As in Australia, Ireland and the U.K., control of spread in the USA has been difficult, even with good control facilities. MRSA now represent a global problem.

3. VIRULENCE

No laboratory tests are available to determine differences in clinical virulence. The emergence of MRSA in Europe in the late 1960s was predominately associated with phage group III strains, often 83A. These strains colonised and sometimes infected postoperative wounds and occasionally caused septicaemia in susceptible patients, but rarely infected healthy staff. They were virulent but differed from previous infections with phage type 80 strains which caused primary sepsis in healthy staff and patients. Nevertheless, no significant difference was found between methicillin-resistant *Staphylococcus aureus* (MRSA) and methicillin-sensitive *Staphylococcus aureus* (MSSA) in animal virulence tests or in laboratory virulence factors.
A similar difficulty has arisen with the 'new' MRSAs which emerged in the late 1970s. These are still predominately phage group III strains, although many are non-typable by the conventional set of phages and require the use of other phages. They are more resistant than the original MRSA and cause severe infections of wounds and burns, and at the sites of invasive devices in the lower respiratory tract may cause septicaemia. Many strains are obviously as virulent as sensitive strains. In 88 episodes of septicaemia due to MRSA in Irish hospitals involving 82 patients, 33 of those episodes were considered to be the direct cause of death.

Although MRSA is common in southeast Asia, invasive infection is uncommon. In Hong Kong, no difference was found between MRSA and MSSA in terms of clinical infection or in animal studies. Of 154 bacteraemias, 74 were caused by MRSA and 80 by MSSA. Other studies have shown similar results. Methicillin resistance is therefore not an indication of virulence. On the contrary, it has been suggested that MRSA is usually of low virulence, since it does not cause primary infections and is almost always associated with underlying lesions. However, it seems more likely that the spectrum ranges from low to high virulence. Group III phage types in general tend to be good colonisers of wounds, but occasionally causing wound infections and septicaemia, and are mainly present in hospitals; their virulence characteristics differ from most of the type 80 strains. Primary infections of MRSA in hospital staff have rarely been described. Although strains probably differ in virulence, clinical infection depends mainly on the state of the host and the type of lesion. Some of the epidemic strains colonise elderly hospitalised patients with pressure-sores and rarely cause clinical infection. Patients with burns in the U.S. were frequently clinically infected with MRSA, but less so in burns units elsewhere. Although virulence cannot be detected in laboratory tests there is also some clinical evidence suggesting that virulence has been acquired by MRSA from a more virulent MSSA, although the mechanism is not known.

4. SPREAD OF INFECTION

4.1 Genetic Transfer of Resistance

The gene responsible for intrinsic methicillin resistance is mecA which encodes for penicillin-binding protein PBP2a. This occurs worldwide and was present in the earliest strains identified. An evolutionary spread from an ancestral gene starting point with episodes of horizontal transfer and transformation contributing to spread in natural staphylococcal populations has been postulated. Whether new clones spread worldwide from a single starting point, or from a number of similar starting points in different populations, is not known, but similar strains were isolated in different countries before methicillin was in clinical use. As already discussed, epidemic strains are spreading from hospital to hospital in most countries and it is not understood why they sometimes decline and are replaced by new clones which spread to a varying extent. A single multilocus enzyme genotype has been postulated for strains which emerged in Europe in the 1960s and which differ from the new strains in the U.K. and Australia, which also differ from those in the U.S.
4.2 Transmission of Organisms

Transmissibility is difficult to assess. Some strains, such as EMRSA-1 in southeast England, appear to spread readily, and others not at all. As with virulence, there is no laboratory test to show why some strains appear to be more transmissible than others, therefore all strains must be treated as potentially transmissible. Person to person represents the main mode of spread.

Early studies on \textit{S. aureus} in infant nurseries have clearly demonstrated that handborne transmission was the main mode of spread, although airborne spread could occur\cite{86,87}. Evidence has not so readily been obtained from adult studies, but it is likely that the results of the studies in infants are applicable to other types of patient.

Staphylococci are usually shed, not directly from the respiratory tract, but from skin scales\cite{88}. Shedders of large numbers (dispersers) tend to be mainly persons with desquamating skin lesions\cite{89,90,91}. Males are more likely than females to be heavy dispersers and to be perineal carriers of \textit{S. aureus}\cite{92}. Airborne transmission is likely to occur from dispersers. \textit{S. aureus} is normally found in two main carriage sites, the nose (20-30\%) and, to a lesser extent, the perineum (3\%)\cite{70,93}; hands are likely to be contaminated from these sites, but are rarely colonised\cite{94}. Heavy environmental contamination of bedding and wound dressings etc. may be associated with airborne transmission, but is more likely to be associated with handborne spread, and possibly via protective clothing of staff\cite{95,96}. Although shedding is less likely to be associated with nasal carriage alone, large numbers of organisms in a carriage site, particularly if multi-resistant, may be responsible for dispersal\cite{97}. The simultaneous emergence of a number of nasal carriers of \textit{S. aureus} of the same phage type in a ward is further suggestive of airborne spread. Staff nasal carriers of the "old" epidemic strains were infrequently responsible for direct spread of infection, but tended to be victims\cite{88}.

Detailed microbiological studies have been few in recent years and heavy environmental contamination has rarely been reported, except in burns units. A detailed study over 10 weeks in a burns unit showed peak counts in the air, on floors and other surfaces in patient wards, but were low in adjacent rooms\cite{99}. Isolation of MRSA from a blood pressure cuff and a shower in another burns unit was thought to be significant\cite{100}. Another study of environmental contamination during an MRSA outbreak showed widespread low-level contamination, mainly around the beds of infected patients, but not on nurses’ aprons\cite{101}. The role of the environment, therefore, remains uncertain\cite{102}.

Staff working in units involved in the "new" MRSA outbreaks may carry the strains in their nasal passages, but staff carriers are rare (1-6\%) and many are transient carriers\cite{89,102,103,104}. Although transmission of infection from a staff nasal carrier has been reported\cite{105}, and temporary staff have possibly transferred strains between hospitals, this is uncommon but cannot be excluded. For this reason, in outbreaks of MRSA staff carriers should be treated if possible.

Most reports suggest that the hands of staff are the main route of transmission of MRSA\cite{48,49,51,70,106}, often based on the absence of organisms in the inanimate environment,
and their occasional presence on hands after treating an infected patient. *S. aureus* is commonly isolated from hands of staff in dermatological wards and burns units where heavy dispersal is frequent.

In summary, it is likely that spread of MRSA occurs in the same way as that described previously for epidemic MSSA strains. The main sources are colonised or infected patients introduced from another hospital or country but occasionally by a member of staff moving from one hospital to another. Heavy dispersers are likely to be the main source, but spread can also occur from staff or patient nasal carriers. Other carriage sites, e.g. perineum, skin of buttock area, may be more important than the nose (personal observation), and wound dressings may also cause transient carriage.

Although hands of staff are the main route of transmission, airborne or spread on fomites could occur from heavy dispersers, particularly in burns or dermatological wards. The inanimate environment usually has a minimal role, but organisms can be dispersed from grossly contaminated bedding or curtains and contaminate hands or clothing of personnel. Contaminated medical equipment, such as stethoscopes, may be responsible for transmission. Failure to change gloves between patients may also lead to transmission. The origin of strains causing an outbreak is not always clear and there is sometimes evidence of a colonised patient without previous hospital contact bringing an epidemic strain into a hospital. At present, spread in the community outside of residential establishments is rare, although there have been reports of infections in drug addicts.

As with virulence, different strains of MRSA vary in their transmissibility. There is some evidence that pigmented epidemic MRSA strains in Australia are more resistant to drying than non-epidemic strains, but the relevance of this to transmissibility in other countries remains uncertain.

5. **PREVENTION OF SPREAD**

Methicillin-resistant *S. aureus* is usually introduced into one hospital from another where the strain is endemic or epidemic, and the source patient is usually infected or has a colonised lesion, e.g. pressure-sores, burn or dermatitis. A patient or a member of staff with a healthy colonised carriage site, e.g. nose or perineum, is less likely to initiate an outbreak, but is more difficult to detect. If the original source is not immediately identified, spread can occur without detection, particularly if there are no clinical infections. A good microbiology service is, therefore, essential as eradication becomes increasingly difficult as more wards or units are involved. A summary of 46 published reports showed that eradication was achieved mostly in hospitals with fewer than 20 cases, whereas only 10% of hospitals with 40 or more cases were successful. However, eradication of an endemic strain can be expensive and may not be worthwhile if the organism is widely dispersed in a hospital but is not in a high risk unit and is not causing many clinical infections.

Although many countries have a problem with MRSA, most have been able to identify imported cases and restrict spread, and several have not yet observed any significant spread. This may be due to the fact that epidemic strains have not been introduced or detected, or that these countries have more effective infection control procedures or
antibiotic policies than some of the affected countries, although this is unlikely. Western Australia has maintained a low level of MRSA through rigorous screening of patients and hospital staff from other parts of the country but the spread of a new strain is currently causing problems.

National guidelines for the control of outbreaks have been published, and their use has led to MRSA eradication in many hospitals but the lack of evidence from controlled studies has hampered their universal acceptance. A number of reports of eradication have been described, mostly involving aggressive screening and isolation or cohort nursing of infected patients, good hygiene techniques, and antiseptic treatment of nose and skin. However, these methods have not always succeeded in preventing spread. In a summary study of 256 hospitals in the U.S., most of them reviewed laboratory reports, used careful handwashing and single rooms to control spread.

6. STRATEGIES FOR CONTROL

The choice of a strategy depends on:

(a) The type of unit, e.g. medical, or intensive therapy unit (ITU)
(b) The potential virulence of the organism (number and severity of clinical infections)
(c) The transmissibility of the organism
(d) Whether the strain is already widely distributed in the unit or hospital
(e) Whether the strain enters a hospital which has no other cases
(f) The facilities and resources available
(g) Antibiotic usage in the hospital

Efficient infection control in a hospital requires:

(a) An infection control committee
(b) A team consisting of an infection control officer (usually a physician) and an infection control practitioner (usually a nurse)
(c) A system should be set up for the rapid detection of infection and resistant organisms (surveillance)
(d) A mechanism is required for communicating with other hospitals if patients with MRSA are transferred
(e) The setting up of appropriate policies, including a policy on antibiotics

The latter should be set up and implemented and staff trained in their use. An efficient microbiological laboratory is also a major requirement. Although it is difficult to define specific antibiotics which select MRSA, antibiotics play a major role in selecting resistant strains.

The antibiotic policy should indicate the rational use of antibiotics and their use where appropriate. The third generation cephalosporins may be selective agents, but others, such as quinolones, mupirocin, gentamicin, or erythromycin may also select resistant strains.
The occurrence of severe clinical infections in an intensive care unit, or the introduction of a single case in a hospital in which MRSA was absent, require eradication procedures if possible. The presence of several colonised patients in a long-term care unit usually requires only basic hygiene procedures. According to the availability of resources, three possible strategies have been described by Spicer\(^2\) - minimal, intermediate and maximum responses. A consensus modification is suggested here\(^3\).

6.1 Minimal Response

This may be appropriate for hospitals with limited facilities and resources, with relatively untrained staff, or in low risk units with colonised patients and few clinical infections.

**Measures**

(a) Good basic hygiene, especially handwashing
(b) Wearing disposable gloves, if available, for contact with discharging lesions or contaminated dressings or equipment
(c) Minimal ward transfers of patients and staff

Although these measures may reduce the spread, they are unlikely to completely prevent transmission of an epidemic strain.

6.2 Intermediate Response (if resources are available)

Patients with infected lesions should be isolated in single rooms or in an isolation unit, or should be cohort nursed in a special ward, if these facilities are available.

Handwashing, as above, preferably with an antiseptic. An alcoholic handrub (see p. 11) is especially useful in the absence of a good water supply or running water.

Gloves and a gown or plastic apron for close contact with patients and their immediate surroundings.

6.3 Maximum Response (eradication programme)

This is preferred if infected patients are in special units such as an intensive therapy unit (ITU), or surgical, orthopaedic or neonatal wards, or on the first appearance of an epidemic strain in a ward or hospital. Adequate facilities, resources and trained staff are required for eradication procedures.
Measures

(a) Screening of all patient lesions and carriage sites (see Appendix)
(b) Isolation in single rooms, or in an isolation unit, or
cohort-nursing in a special ward for all carriers and
infected patients
(c) Covering lesions with bacteria-impermeable dressings;
this helps but not all sites can be covered
(d) Treatment of nasal carriage sites with mupirocin
(e) Daily bathing and washing of infected patients with
an antiseptic detergent (see p. 12)
(f) Treatment of throat, vaginal or rectal carriers with a
combination of rifampicin and fusidic acid (or
trimethoprim or ciprofloxacin) if strain is sensitive
to both these agents

If several cases in a ward have clinical infections, and if isolation facilities are
insufficient, it may be necessary to close the ward to new admissions. If there are more than
three or four infected patients or carriers, all patients in the ward should bathe or wash with
antiseptic detergent, irrespective of whether they are colonised or infected (see p. 12). Staff
should be screened for infection and nasal carriage and carriers treated. As already
described, handwashing with an antiseptic, wearing gloves and a gown or plastic apron for
close contact with patients, are essential.

Procedures on initial detection of MRSA in a hospital
with no other cases: Single infected patient or carrier

- Isolate in single room (or send home), treat with
nasal and skin antiseptics and improve basic hygiene
precautions.

More than one infected patient or carrier in a surgical
or high-risk ward
(a) Screen all patients and staff: lesions and carrier site
(noses in staff)
(b) Isolate all patients with positive screening results in
single rooms, an isolation unit or cohort in a special
ward
(c) Treat all infected or colonised patients and staff with
nasal ointment and antiseptics, where appropriate
(d) Avoid transferring patients or staff to other wards
6.4 Endemic Situation

If MRSA contributes over 5-10% of staphylococcal isolates distributed over more than one unit, consider cost-effectiveness of eradication procedures. If there are no clinical infections, introduce improved hygiene measures only and avoid transfers between affected and unaffected wards. Eradication measures may be required if MRSA is present in the intensive care unit, or if clinical infections are present in surgical, orthopaedic or neonatal wards.

6.5 General Measures

(a) Bed linen should be handled carefully and transported in a sealed bag or container.

(b) Clinical waste should be sealed in a plastic bag or container and preferably incinerated. After a ward has been cleared of infected or colonised patients, wash surfaces, not walls or ceilings, preferably with a disinfectant (effective against S. aureus).

(c) Equipment used on a colonised or infected patient, e.g. stethoscopes, blood pressure cuffs, should be decontaminated with an alcoholic or aqueous disinfectant before use on another patient.

(d) If transferred to another hospital, an MRSA positive patient or a patient from an affected ward should be reported to infection control staff in the receiving hospital.

(e) Patients can be transferred to a long-term care establishment before clearance, since MRSA are unlikely to cause infection in relatively healthy people. The nursing home staff and relatives should be informed of these minimal risks, and nursing home staff should have some training in aseptic techniques.

(f) Moving patients to other departments (e.g. physiotherapy) should be avoided if possible; if such a move cannot be avoided, the staff in these departments should be instructed in the hygienic techniques required. Transfer of patients or staff to other wards in a hospital is now a common procedure, and is a major factor in increasing the spread of MRSA.

(g) The hospital records of carriers or infected patients should be clearly marked, irrespective of negative clearance swabs, so that they are quickly identified on admission to another hospital or on readmission.

6.6 Staff Handwashing or Disinfection

Hands should be washed with soap and running water, or preferably with an antiseptic. All surfaces of the hands should be covered with soap or the aqueous disinfectant and a small amount of water. Washing with the agent should continue in accordance with the manufacturer’s instructions before rinsing and drying with a paper towel or clean hand towel. The use of 60-70% isopropanol or ethanol with an emollient (e.g. 0.5-1% glycerol),
with or without an added antiseptic, is an effective alternative to the use of soap; add approx 3ml to cupped hands, cover all surfaces and rub to dryness.\textsuperscript{130}

6.7 Topical Treatment of Carriers

Although controlled studies provide little evidence of the effectiveness of treating carriers in reducing the spread of infection, it is reasonable to accept that a reduction in the number of sources of staphylococcal dispersal should reduce spread of infection.

6.8 Treatment of Nasal Carriers and Skin Disinfection

The most effective treatment is mupirocin ointment applied to the anterior nares 3 times daily for 5 days.\textsuperscript{130 131} This course can be repeated, but there is a risk of resistance emerging.\textsuperscript{132 133 134} Less effective alternatives, which should be considered after two courses, include chlorhexidine (1%), neomycin (0.5%) and chlorhexidine (0.1%), bacitracin (500 units/g), or povidone-iodine (0.5%) creams or ointment.\textsuperscript{117 118} The topical use of antibiotics which may be required for systemic use, e.g. ciprofloxacin, fusidic acid, or gentamicin, should be forbidden. Mupirocin cream may be applied to infected MRSA lesions, but it should not be used on large areas (e.g. burns or pressure sores) and treatment should not exceed 5 days.

\textit{Staphylococcus aureus} from carriage sites may disseminate over the skin surface. Washing and daily bathing with an antiseptic-detergent is advised (e.g. chlorhexidine 4%, triclosan 2%, povidone-iodine 7.5%, hexachlorophene 2-3%). This should be applied to moist skin, as recommended by the manufacturer, before rinsing. Direct application to colonized skin sites (e.g. perineum and buttocks area) is of particular importance. Hair should be washed at least twice a week with an antiseptic detergent. Antiseptic bathing and washing may be extended beyond 5 days, but eradication is unlikely if a colonised lesion remains.

Staff nasal carriers (without lesions) may return to work during mupirocin treatment.

6.9 Treatment of Clinical Infection

Vancomycin or Teicoplanin are the antibiotics of choice for severe infections. Depending on the sensitivity of the organism, other agents can be used, but resistance may rapidly emerge, especially to fusidic acid, rifampicin and ciprofloxacin.\textsuperscript{71 118 135} If agents other than vancomycin or teicoplanin are preferred, combinations of at least two agents should be used. For severe infections, the addition of another agent to vancomycin or teicoplanin, for which tissue penetration is not good, is also desirable.

7. COSTS OF CONTROL AND INFECTION

MRSA infections can be expensive in terms of antibiotic therapy, isolation facilities, materials, and length of hospital stay. Estimates of $20,000 - $114,000 have been made for outbreaks, and from $28,000 to $1,600,000 per year for endemic infections.\textsuperscript{112} Similarly, the cost of an outbreak in a badly affected hospital in the U.K.\textsuperscript{102} has been estimated at
£250,000. In one of the few studies actually measuring costs, an outbreak involving 30 patients over 5 weeks cost £13,000\textsuperscript{136}. This did not include costs of isolation or increased length of stay.

8. PRINCIPLES OF PREVENTION OF SPREAD OF MRSA

(a) Set up infection-control organisation, e.g. committee and team. Produce policies and train staff - include rational, cost-effective use of antibiotics and provide effective microbiological service

(b) Minimise ward transfers of staff and patients. Inform other hospitals, nursing homes or units if patient is transferred. Colonised patients can be transferred to a long term care establishment. Mark medical records of infected and colonised patients

(c) Ensure early detection of cases, especially if admitted from another hospital with known epidemic or endemic MRSA

(d) Isolate infected or colonised patients in a single room, isolation unit or cohorting in a larger ward (or send home)

(e) Enforce handwashing by staff after contact with infected or colonised patients, preferably with an antiseptic

(f) Use gloves for handling MRSA-contaminated materials, or infected or colonised patients. Wash hands after removing gloves

(g) Wear gown or apron when handling contaminated materials, or infected or colonised patients

(h) Treat nasal carriers with mupirocin (for alternatives see p. 12). Daily wash or bathe carriers or infected patients with antiseptic detergent

(i) Ensure careful handling and disposal of linen and waste, and terminal disinfection of isolation rooms

The extent of application of these principles depends on the availability of resources and on the severity of the outbreak. Minimal precautions are required for colonised patients with few clinical infections in units, other than high risk units. Maximum precautions are required for severe clinical infections in high risk units, or for the prevention of initial spread in an MRSA-free hospital.

The reason for the initial reduction of MRSA in Europe, and its later simultaneous re-emergence in many countries throughout the world, is unknown but it seems probable that antibiotic usage plays a role. There is as yet no evidence that any changes in policy will influence the spread of MRSA, but further studies on policies are required. However, rational use of antibiotics, in association with effective infection control procedures, should help to reduce this spread.