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Meticillin-resistant *Staphylococcus aureus*

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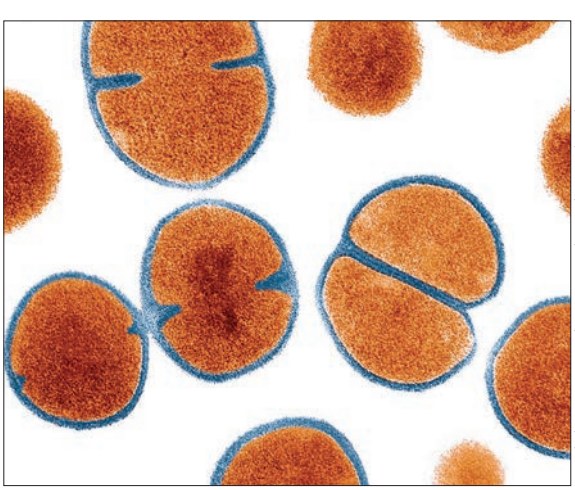
Meticillin was introduced in 1959 to treat infections caused by penicillin-resistant *Staphylococcus aureus*. In 1961 there were reports from the UK of *S aureus* isolates that had acquired resistance to meticillin (meticillin-resistant *S aureus*, MRSA). Similar MRSA isolates were soon found in other European countries, and later from Japan, Australia, and the USA. Today MRSA is a major cause of hospital-acquired infections, and a serious public-health concern. In this forum, we present different perspectives from across the globe to better understand the complexity of the problem, and examine the challenges that individual countries face in trying to control the spread of MRSA.

USA

The epidemiology and the clinical management of MRSA infections have continued to evolve in recent years in the USA. The prevalence of MRSA has increased progressively since the early 1980s, and by 2002 MRSA accounted for nearly 60% of nosocomial *S aureus* infections acquired in intensive-care units.[1] MRSA strains have been reported to account for 30–62% of nosocomial *S aureus* bloodstream infections and 42–60% of *S aureus* surgical-site infections.[2–7] In some facilities, the proportion of health-care-associated *S aureus* infections caused by MRSA is even higher. Vancomycin-intermediate *S aureus* (VISA) strains, which have vancomycin minimum inhibitory concentrations (MICs) of 8–16 mg/mL, have continued to cause occasional health-care-associated infections, although transmission within health-care facilities of such strains has seldom been documented.[8] At least three well-documented isolates of vancomycin-resistant *S aureus* (VRSA) that have vancomycin MICs of 32 mg/mL or greater have been recovered from patients in the USA.[9] Although it is possible that the relatively high frequency of co-colonisation by vancomycin-resistant enterococci (VRE) and MRSA among patients in the USA may create more opportunities for in-vivo transfer of the *vanA* gene complex from VRE into MRSA strains, it is not known if this has affected the frequency of VRSA in the USA.

By contrast with the uncommon occurrence of VISA and VRSA, MRSA strains that are still classified as susceptible to vancomycin (ie, MICs of 1–4 mg/mL) have caused an increasing number of health-care-associated infections that respond poorly to vancomycin therapy.[8,10,11] The poor response to vancomycin therapy in such cases appears to be associated with several strain characteristics. Patients infected with MRSA strains with vancomycin MICs of 1–4 mg/mL have responded to vancomycin therapy less frequently than patients with infections caused by strains with MICs of less than 0·5 mg/mL.[10] In some cases, poor clinical responses may have been due to strains with hetergenous resistance to vancomycin—so-called hetero-VISA.[6] Fowler and colleagues[14] found that MRSA bloodstream infections that persisted for more than 7 days despite appropriate vancomycin therapy were significantly more likely than short-duration MRSA infections to have been caused by strains that exhibited (1) higher rates of survival in vitro after exposure to thrombin-induced platelet microbicidal protein (p=0·005), (2) defective delta-lysin production (suggestive of loss of accessory gene regulator [*agr*] function; p=0·057) and (3) *agr* type II (p=0·037). In two prospective randomised trials of treatment of ventilator-associated pneumonia (VAP), vancomycin therapy was significantly less effective than treatment with linezolid (p=0·001) among a subset of patients with VAP caused by MRSA.[12] Unfortunately, the microbiological characteristics of MRSA from these pneumonia studies were not described in detail. The above trends suggest that although vancomycin remains the drug of choice for most serious health-care-associated MRSA infections, clinicians in the USA may need to consider the use of other agents—eg, linezolid, daptomycin, or tigecycline—in some clinical situations based on the characteristics of the infecting strain and the body site affected.

Another major change in the epidemiology of staphylococcal infections in the USA is the rapid emergence of community-acquired MRSA strains since the late 1990s.[13–16] Although such infections have been more common among population groups such as young children, native American and Pacific islander communities, prisoners, military personnel, men who have sex with men, intravenous drug users, and individuals involved in amateur or professional competitive sports, spread within the general community is likely occurring.[13,15–17] A relatively small number of unique



Biomedical Imaging Unit, Southampton General Hospital/Science Photo Library

Coloured transmission electron micrograph of dividing MRSA

strains appear to be responsible for many of the community-acquired MRSA infections occurring in the USA.[17] Most of such strains contain the mobile genetic element staphylococcal cassette chromosome *mec* (SCC*mec*) type IV, which is relatively uncommon among health-care-associated MRSA strains in the USA.[18] Emergence of community-acquired MRSA has also required that clinicians alter their approach to empiric treatment of community-acquired skin and soft tissue infections. Physicians have been encouraged to routinely culture skin lesions to determine if community-acquired MRSA is the cause, and in geographic areas where community-acquired MRSA are relatively common, empirical therapy of such infections with clindamycin, trimethoprim-sulfamethoxazole (co-trimoxazole), doxycycline or minocycline, or linezolid is becoming common. If empiric clindamycin is administered, testing community-acquired MRSA isolates for inducible clindamycin resistance by using the "D-test" is recommended.[19]

By contrast with the Netherlands and some other parts of northern Europe, no standard set of measures has been adopted in all health-care facilities in the USA for controlling transmission of MRSA. Measures recommended by the Society for Healthcare Epidemiology of America for controlling health-care-associated MRSA include the use of screening cultures to detect colonised patients, placing patients in private rooms or cohorting patients, wearing gloves for room entry, gowns for substantial contact with patients or their environment, and hand hygiene before and after patient contact.[20] However, there is considerable debate among experts in the USA about whether or not the use of screening cultures to detect patients at high risk of MRSA is necessary or practical in all health-care settings. Given the considerable body of evidence that screening cultures, when combined with contact precautions, are beneficial and cost-effective,[20–22] it is disconcerting that a recent survey of infectious disease consultants found that only 50% of 463 respondents favoured the use of screening cultures to detect multidrug-resistant pathogens, and only 30% worked in facilities where screening cultures were routinely done.[23] The costs of surveillance cultures, potential logistic problems that may result from an increased number of patients requiring isolation, and lack of controlled trials demonstrating the efficacy of screening cultures are often cited as concerns by those who do not use screening cultures. Further studies are necessary to establish the relative efficacy of control measures such as screening cultures, cohort nursing, increased staffing levels, and improved hand hygiene adherence rates in controlling transmission of MRSA in health-care facilities.[24] At present, there is no consensus regarding which measures are most appropriate for reducing transmission of community-acquired MRSA in community settings and for preventing the spread of these strains in health-care facilities.

Conflicts of interest

In the past year I have served as a consultant to Dial Corporation and Woodward Laboratories, who produce hand hygiene products, including alcohol-based hand rubs and soaps. I am currently a consultant to GoJo Industries.

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UK

MRSA was first described in England in the early 1960s, just months after meticillin had been introduced into clinical practice. MRSA has waxed, waned, and waxed again over the following decades. The International Union of Microbiology and WHO's staphylococcal centre is based in the Laboratory of Healthcare Associated Infection of the Health Protection Agency (HPA), and was the first to identify and number epidemic MRSA strains (EMRSA 1–17), plot their spread, and identify the existence of other epidemic MRSA strains in Europe as part of the HARMONY network project.[25] Community MRSA are evident in England but have not yet emerged to be the problem encountered in some other countries.

In the early 1990s, about 2% of *S aureus* bacteraemias were due to MRSA; the mean figure is now about 45%, although there is a large range, with some hospitals encountering the organism infrequently. Current English data show that the occurrence of meticillin-sensitive strains has also increased, so merely focusing on the percentage of total *S aureus* bacteraemias can be misleading. Ever since the organism was first described, hospitals have continued to vary in MRSA occurrence within and between different cities and in different wards within the same hospital. The reasons are complex and may include aspects of the reporting system; a comparison of reporting methods is underway. We know that the current prevalent UK epidemic MRSA (EMRSA strains 15 and 16) differ genetically from their predecessors and also contain more or different toxins. However, we still do not understand why certain MRSA strains have this epidemic potential. When such strains spread to other countries they seem to exploit the more stressed or less "infection control compliant" hospitals or wards.

MRSA are opportunistic pathogens colonising more patients than they infect. The patient case mix has also changed. MRSA has always preferably colonised and infected elderly people. Improved nutrition and medical advances has meant that elderly patients are now admitted to "high-risk" units—eg, cardiovascular and orthopaedic wards with periods of care on intensive care units. Such units can then "carousel"

MRSA-affected patients to other parts of the hospital, spreading the organisms elsewhere. There is also MRSA spread between orthopaedic wards and residential or nursing homes, which now care for more severely ill patients. Another change has been the increasing involvement of paediatric populations; this is being studied specifically. It is interesting that obstetrics and paediatrics had encountered MRSA infrequently in previous decades in the UK. Perhaps the development of mixed specialty wards has facilitated its introduction into this population?

Implementation of effective measures is being deleteriously affected by other changing environmental factors. Reduced hospital bed numbers have resulted in increased interward transfers of patients, which have been shown to increase the risk of MRSA acquisition. Decreased lengths of stay have resulted in patients being discharged before they present with MRSA infections. We have thus reduced the effectiveness of our alert organism laboratory surveillance systems. Our data also show that inter-city transfers of patients has encouraged national MRSA spread. Bed occupancy in many hospitals is over 90% and in some parts over 100%. Some UK infection-control teams have problems closing MRSA-affected wards because of the pressures on waiting lists. However, the relation between bed occupancy and MRSA rates is not clear-cut.[26]

Insufficient numbers of skilled staff further compounds the problem. Studies have shown that compliance with infection-control practices decreases as workloads increase, resulting in more MRSA cross-infection. These practices include MRSA screening, effective hand hygiene, wound and intravascular/urinary device care, and appropriate isolation measures. When we did an intra-UK comparison of hospitals in 1995, those that were better able to control MRSA outbreaks had fewer delays in identifying MRSA patients (28·6% *vs* 50%), fewer inter-hospital transferred patients (9·4% *vs* 29·4%), and no problems with mupirocin resistance (0% *vs* 14·7%) compared with those less able to control the problem. A recent English MRSA systematic review[27] concluded that there were many problems with the quality of the reviewed papers. Absence of evidence should not be taken to mean that there is an absence of effect. The authors emphasised that the current guidelines for MRSA control should be followed until evidence emerges that other approaches are effective. Prescribing of certain antibiotics probably contributes to the acquisition of MRSA, although the evidence for this is not clear-cut. The authors indicated the ways in which better studies could be designed to inform the most cost-effective means to produce sustained improvements in compliance.

MRSA control guidelines were first written in 1985 and were similar to the "search and destroy" approach used in non-endemic countries. In 1998 we revised them in the light of the endemic problems encountered in many English hospitals.[28] There has been much debate as to how to best control endemic MRSA and other writers in this Forum have outlined many of these issues. Our analyses of the current situation will further inform the most effective MRSA control measures. New guidelines have been written and a consultation on them is underway.

Several interventions will be required. The Department of Health and the HPA in consultation with many other bodies and health-care workers are introducing a suite of initiatives with various performance indicators and outcome measures that should enable improvements in infection control. However, these initiatives will require substantial funding. Multidisciplinary involvement will be crucial, as well as ownership of infection control by all health-care workers and sharing of good practice. There are clearly many issues that need to be discussed with policy makers; bed managers also need to work closely with infection-control teams. In some parts of England MRSA-free wards are being created, elsewhere MRSA-free or fast-track orthopaedic hospitals are being assessed.

I believe that effective control and real reductions in MRSA will be possible. Screening strategies are critical—eg, planned screening and eradication of MRSA before admissions, monitoring of acquisitions on high-risk units and among patients who have been in hospital for prolonged periods (ie, more than a week), and rotating screening programmes on wards to provide feedback data to inform interventions such as hand hygiene improvement campaigns. A good example of this is the Cleanyourhands campaign, which uses a multifaceted approach including the use of alcohol handrubs and patient empowerment. Rapid MRSA detection systems are being examined for cost-effectiveness. Many systems have been used to isolate patients—eg, an open ward, side rooms, four-bedded cohorting, or an isolation ward. Whatever strategy is used should be validated by screening strategies. Modelling studies have further informed isolation strategies.[27]

The HPA and others have done much to ensure that the news media are well informed about MRSA and have provided leaflets to educate the public. However, we will also need to do more to look at infection-control standards in nursing homes and to plan the eradication of MRSA from patients better after discharge.

Conflicts of interest

I declare that I have no conflicts of interest.

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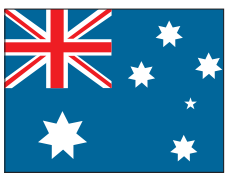
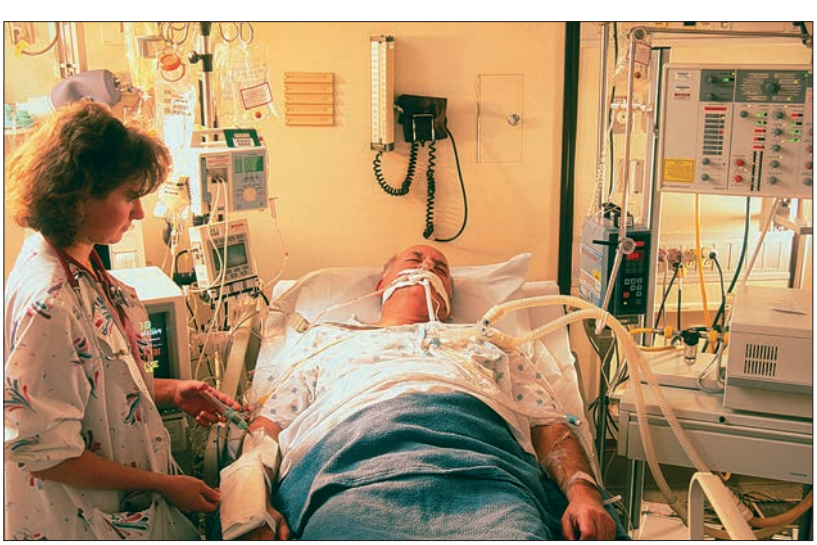


Australia

Epidemic MRSA has a long history in Australia. The bacterium was first isolated in 1968 in Sydney and spread rapidly through teaching hospitals over the next 10 years, such that by the end of the 1980s the prevalence was 10–25% in hospitals in the cities on the eastern side of Australia. Annual surveillance studies by the Australian Group on Antimicrobial Resistance have allowed us to track the evolution of both epidemic and community MRSA for the past 18 years. The current prevalence (2003) for multidrug-resistant epidemic MRSA varies for the state capital cities, and is approximately 35% in Sydney, 22% in Melbourne, 16% in Brisbane, 14% in Adelaide, and 3% in Perth. Recent epidemiological typing studies have enabled the identification of these epidemic strains as predominantly ST239-MRSA-III (UK EMRSA 1, 4, 11, Vienna, Portuguese/Brazilian clones) with two variants, one in Melbourne and Adelaide and the other in Sydney, Canberra, and Brisbane.

See http://www.antimicrobial-resistance.com

Active screening and infection-control policies initiated in the early 1980s following a single hospital outbreak have prevented the establishment of epidemic MRSA in any Western Australian hospital. Since 1997, increasing numbers of ST22-MRSA-IV (UK EMRSA 15) have been detected clinically, on screening, and in the annual surveillance studies. This non-multidrug-resistant clone is the major epidemic strain in Western Australia, where it comprises 21% of all MRSA isolates and 80% of all epidemic strains. A similar trend is occurring on the eastern side of Australia, with Sydney having the highest prevalence of this strain (15% of all MRSA). Nurses coming from the UK are an important source of these isolates, which are often detected on pre-employment screening. This clone has also become established in many long-term care facilities. In addition to nosocomial epidemic MRSA we have been documenting the evolution of true community-acquired MRSA strains in Australia over the past 20 years, such that now we have at least 23 clones that have evolved independently around the country. It is somewhat ironic that Western Australia, the state with the lowest rate of noscomial epidemic MRSA, should now have the highest rate of community-acquired MRSA (75% of all MRSA isolates). These strains, although frequent in admitted patients, rarely seem to be transmitted to others in the hospital. When identified, patients colonised or infected with community-acquired MRSA are managed with enhanced precautions (single room if possible, attention to hand hygiene, contact precautions, and extra cleaning during admission and on discharge). To date, we have not had any major hospital outbreak with community-acquired MRSA, despite an increasing prevalence in the community.



Blair Seitz/Science Photo Library

Intensive care units are high-risk areas for MRSA

My experience with MRSA has been as a Western Australian, where we have successfully used a "search and destroy" policy for at least 20 years. It is state policy that any patient who has been hospitalised outside the state in the preceding year be isolated and screened for MRSA before joining the general hospital population. In addition, staff who have worked clinically outside Western Australia are also screened pre-employment. This screening has led to my colleagues in Sydney, Melbourne, and Brisbane calling us "fortress WA". We have had a number of outbreaks over the years, particularly in my own hospital, which has a lack of single rooms, but swift screening of contact patients and staff, isolation of colonised patients, attention to hand hygiene, and enhanced ward cleaning has terminated the outbreaks rapidly. We also routinely screen all patients in high-risk areas (intensive care, burns, vascular, and spinal units) on admission, discharge, and after prolonged stay. Decolonisation is initiated for persistently colonised staff and patients likely to have frequent readmissions. In general, topical hexachlorophene or triclosan together with mupirocin nasal ointment is used. However, if oral carriage is detected or the topical regimen fails, systemic therapy with two agents is given. I cannot speak for my colleagues on the other side of Australia who have lived with endemic nosocomial MRSA for many years, but I believe that there are a variety of practices mostly aimed at containment rather than eradication. In Brisbane, where the prevalence has been very high, rates have dropped substantially with the move to new hospital accommodation and intensification of infection-control procedures.

It is perhaps easiest for those of us who do not have endemic nosocomial MRSA. We have a very defined end point—no endemic MRSA—that we wish to achieve. For those with endemic MRSA, realistic end points for any containment programme must be established and measures instigated to ensure the attainment of those outcomes. Containment or eradication is important—we are all aware of the emergence of VRSA carrying the *vanA* gene complex. The coexistence of MRSA and VRE

provides the environment for gene transfer. Policies for the control of both these organisms are therefore of paramount importance.

Community-acquired MRSA presents a new challenge. Fortunately in Western Australia, most of the community strains are Panton-Valentine leucocidin (PVL) negative. The infections seen are therefore of similar severity to those caused by susceptible *S aureus*. However, there are disturbing data indicating that our most frequent community-acquired MRSA clone can, and has, acquired PVL on several occasions. We are currently contemplating what community strategies should be implemented, in particular whether we should follow the example of Denmark where a search and destroy policy has been used within the community. It would not be feasible for us to do this with all our community-acquired MRSA isolates but it may be possible for those with PVL. This toxin is carried on a prophage and is therefore potentially mobile. If we can prevent wide dissemination of the PVL genes we could perhaps limit the associated disease severity.

The Australian public is very aware of "the golden staph" tag by which the press has labelled MRSA. There is episodic press coverage, both print and television, of personal stories and individual hospital problems. However, understanding of antimicrobial resistance of any kind is minimal within the community. Providing and disseminating relevant, understandable information that will change community and prescriber attitudes is a challenge that should be met by our profession, regulatory authorities, and politicians.

Conflicts of interest

I declare that I have no conflicts of interest.

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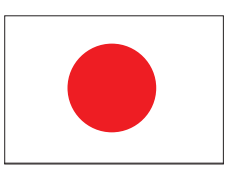
Japan



Japan has one of the highest prevalences of MRSA in the world. Among *S aureus* bloodstream isolates in 2001, nearly 70% were meticillin resistant. To control MRSA in hospitals, it is essential to identify potential MRSA patients immediately after admission. Since microbiological testing usually takes 3–4 days, the identification of those who are at high risk for MRSA carriage is required to decide whether proper precautions should be taken for each new patient.

No mechanism to identify patients within hospitals currently exists in Japan—there is no general database that includes previous medical and laboratory results of patients that can be shared by clinicians between different hospitals. In addition, people can attend any hospital they choose—from a large teaching hospital to a general hospital—without an appointment. Without MRSA screening on admission, this situation makes it difficult to know whether the patient has already been colonised or infected with MRSA in the past.

Ignorance about MRSA is a huge problem among the public and media in Japan. Although there is some interest in the subject, the risks and safety issues surrounding MRSA are generally not that well known. MRSA carriage is seen as a "stigma" for patients and because colonisation with MRSA is not usually differentiated from an infection, the media are quick to generate a scandal and attach blame to hospitals and doctors when MRSA is reported. Hence, most hospitals tend to refuse MRSA-positive patients to avoid potentially damaging repurcussions for the hospital. Moreover, this situation can lead to clinicians hesitating to identify MRSA carriage of patients who are being transferred to another hospital. In many countries it is strongly recommended that clinicians at the transferring hospital should notify MRSA carriage status of the patient to the infection control team at the receiving hospital before transfer. However, this procedure has not been followed stringently in Japan.

An MRSA flagging system to highlight previously identified patients within the same hospital or upon readmission is expected to become available soon to most clinicians.[29] This flagging system needs to be computerised and added on to the individual database in each hospital. However, it is still difficult to share microbiological results through a single medical computer network system. Each hospital needs to develop MRSA flagging software for this purpose. Although Japanese hospitals are extensively computerised, the main purpose of the hospital computer system is for ordering and accounting for medical procedures. The data sorting function from previous laboratory results is usually optional. We have recently developed a small computer programme on our hospital network to indicate an "alert spot" on the individual patient record window. If a patient has a previous history of being MRSA positive, a red-coloured alert spot automatically appears on the computer display. This alert system helps us to recognise whether the patient is a potential or current MRSA carrier without checking any previous microbiological results, which is usually a tedious and time-consuming procedure for busy clinicians and hospital officers. This function will be introduced to a new hospital computer system in the future. Ideally, these data will become indispensable information for inter-hospital transfers via a shared database that should be set up in the future.

An alternate route of importing MRSA into hospitals is from the community.[30] Only a few studies of MRSA prevalence in the community have been published from Japan. One study reported that 35 out of 818 (4·3%) healthy children aged 3–5 years old carried MRSA in their anterior nares.[31] This prevalence of community MRSA

among children is high, and deserves further prevention efforts.

MRSA surveillance is currently mandatory in large general and university hospitals but not in middle to small-sized hospitals that are the most common types of hospital in Japan. For example, geriatric hospitals with less than 200 beds are usually one of the most important reservoirs of MRSA. MRSA-positive patients are sent to us from these types of institutions without information of MRSA carriage. Therefore, it is important that MRSA surveillance should be made mandatory by legislation.

Another less common strain of MRSA is VISA, which was first reported in Japan.[32] Although the hetero-VISA strain (a possible precursor of VISA) was identified in 9·3% of MRSA isolates in seven university hospitals,[33] a new VISA strain has not been identified in Japan so far, because therapeutic drug monitoring has become widely available from both "in-house" and commercial laboratories since 2000. Controlling the use of vancomycin means there is less chance for the emergence of vancomycin-resistant strains.

Educational awareness of MRSA should be provided to all health-care workers as well as the general public, and should be supported by the government or relevant associations and academic societies. MRSA carriage should be notified properly when the patient is transferred from one hospital to the next.

Conflicts of interest

I declare that I have no conflicts of interest.

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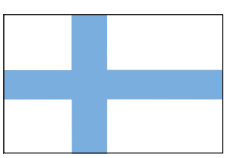

Finland

Finland is a country with low MRSA incidence. The incidence figures are based on mandatory reporting by clinical microbiological laboratories of each new MRSA isolation since 1995 and analysis of MRSA strains at the national reference laboratory at the National Public Health Institute. In recent years, however, we have seen a worrying increase in the number of MRSA cases. The number of reported cases has increased from 120 in 1997 to 1460 in 2004 (from 2·3 to 28·04 cases per 100 000) in a population of 5·2 million. For many years MRSA remained below 1% among invasive cases, but during 2004 we saw the first signs that the figures were worsening substantially. At the same time, the coverage and efficacy of MRSA reporting has remained stable, thus we assume that we are facing a true change.

Strict MRSA prevention measures are taken following each newly identified MRSA case, regardless of whether it is symptomless carriage or infection. In response to three large MRSA epidemics in southern Finland, national MRSA prevention consensus guidelines were adopted in 1995. The updated version of these guidelines was published in 2004.[34] The new guidelines cover both acute care hospitals and long-term health-care facilities, including homes for elderly people. The main principles are promotion of hand disinfection, identification of MRSA risk patients (carriers and contacts of known MRSA cases), rapid microbiological identification of MRSA, contact isolation of MRSA cases, and treatment of MRSA infections. Emphasis is placed on trying to target preventive measures at the very first steps of possible MRSA transmission. According to the guidelines, every patient who has been treated in a hospital outside of Finland during the previous year and is transferred to a Finnish hospital is screened for MRSA colonisation at the time of hospital admission. Patient records of each MRSA case are labelled accordingly, and an "MRSA alert" is also added to electronic patient records in many institutions. These actions have proven to be effective in controlling several rather large hospital MRSA outbreaks in the 1990s. Some of the international MRSA clones have also repeatedly entered our country via patients or health-care workers who have come from abroad, but they have caused few secondary cases or outbreaks.

During the past couple of years, the MRSA situation has changed in Finland. In 1997–99, one-fifth of our cases showed no contact with the health-care system, and were thus considered community-acquired MRSA.[35] Usually, these MRSA strains possess only beta-lactam resistance, carry the SCC*mec* type IV genes, and cause problems in younger age groups. However, the proportion of elderly people with MRSA has increased steadily. In 2004, over 50% of cases were found in individuals aged 75 years or older. In 2002, over half of Finnish MRSA cases were reported in long-term care facilities, and outbreaks are

Klaus Rose/Das Fotoarchiv/Still Pictures

Nursing homes are becoming increasingly common settings for MRSA

occurring in these facilities.[36] These two settings—community acquisition and long-term care facilities—create new and demanding challenges to our MRSA prevention policy.

The Finnish health-care system is currently struggling with increasing output demands and decreasing funding. The nursing staff is often overwhelmed with work, and patient wards are crowded and often lack single-bed isolation rooms, creating problems for infection control. In long-term care facilities, we are witnessing the lack of trained personnel and problems in finding functional placement options for MRSA carriers. There has been a considerable amount of debate about the ethical right to isolate MRSA carriers in the nursing home setting. It is difficult to find a solid answer that would hold for every case. In our decisions about MRSA-positive people we try to respect two basic principles: the patient's right for proper medical treatment and the individual's right to live a normal life.

The actions taken now and over the next few years are crucial in determining how the trend of MRSA in Finland progresses. At present, we still have the chance to prevent the situation from becoming much worse. In 2005, the Finnish government launched a fund for the health districts to update their resources on emerging hospital infection issues, including MRSA prevention. Sweden, Denmark, Norway, Iceland, and Finland have also started a joint initiative, provoked by the Scandinavian Society for Antimicrobial Chemotherapy, to try to find ways to keep MRSA levels below 1% among *S aureus* isolates in each country. At the very least, this cooperative effort will mean that information on the MRSA situation is exchanged, attempts are made to improve MRSA laboratory diagnostics, common reasons for why MRSA is emerging sought, and attempts made to increase awareness among the public and health-care workers. In countries where MRSA case levels have remained low, the only right and ethical decision is to try to fight hard to keep the situation from becoming worse. This battle requires new investments now, but it will save money and resources in the future.

Conflicts of interest

I declare that I have no conflicts of interest.

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Turkey

MRSA emerged in Turkey in the 1980s as a major clinical problem in hospitals, and to date has continued to be one of the most problematic nosocomial pathogens. The extent of resistance varies nationally, regionally, and even institutionally. In addition to meticillin, these strains are also resistant to routinely used antimicrobials, and thus infections caused by such isolates cause serious treatment difficulties.[37]

Unfortunately for Turkey, accurate and recent population-based national surveillance for community-acquired and hospital-acquired drug-resistant micro-organisms does not exist. However, data from sporadic reports of the number of cases suggest an urgent need for surveillance. Available reports provide a fragmented and incomplete picture to guide our understanding of the problem. The most recent and only national resistance screening programme data supported by the Turkish Scientific and Technological Research Council is from 1993. In this study, 1826 clinical isolates both from outpatient and inpatient clinics (including surveillance isolates) from 29 different hospitals were collected and screened. Overall, MRSA resistance varied from 7% to 55% at different centres.[38] This range of resistance may have been due to variations in patient population, hospital care practices, and infection control activities. Other factors—eg, size, locality, and type of hospital—were also contributing factors to the wide disparity in resistance. Among the identified isolates, 178 nosocomial strains were randomly selected for evaluation of the mechanisms of meticillin resistance, and the presence of *mecA* was found to be the most frequent type (94%).[38]

When various other studies from different centres were evaluated up to 1995, it was noted that up to 40% of strains in some places were MRSA. In a further evaluation extending to 1999, this figure rose to 70%.[39] More recently, data from the past 5 years from individual centres across Turkey state the percentage of MRSA strains is 65·5%.[40–43] When tested, all strains were reported to be vancomycin and teicoplanin susceptible but potential emergence of resistance to these drugs should be kept in mind, since this has prompted the overuse of glycopeptides in empirical and even prophylactic therapy.[44,45]

Evaluation of reports showed no correlation between MRSA rates and sex, profession, hospital department, or carriage. It was difficult to evaluate the age distribution and age group at risk. Ideally at each hospital multidrug-resistant strains should be regularly identified. Clonal typing methods should be used to identify the relations between these strains, and to see which strains predominate in the country. We evaluated our hospital's main nosocomial MRSA clone and tried to track the sources of the clonal types in different clinics by pulsed field gel electrophoresis. One major type was identified among their strains. This single clone was compared with another Turkish university hospital's clone and several main international clones including the Iberian and Brazilian clone, and it was found to be different from them.[46] Predominance of this clone or any other clone is not known. This type of evaluation needs to be done by most hospitals. With enough funding a national

epidemiological surveillance group should be established.[47]

Data emerging from various centres indicate that in Turkey—like many other countries—both infections and the rate of MRSA is gradually increasing. The main factors that contribute to this organism's resistance are misuse and overuse of antimicrobials, which include constant pressure on the physician to prescribe antimicrobials when they are not indicated, the patient's failure to finish a prescribed antibiotic regimen, and also the availability of antimicrobials without a prescription. We believe that control of such factors, alongside implementing good infection-control procedures in Turkey, will result in decreasing rates of MRSA. Studies from other countries have shown that surveillance activities—eg, setting up a national/regional system to collect and evaluate data from all centres and updating data on antibiotic resistance patterns that will form the basis for prevention guidelines of nosocomial infections—decrease infection rates by as much as 20%.

The negative impact of nosocomial infections on our health-care system is not well documented. Data obtained from limited number of studies are not suitable for comparison with each other and neither are data from other countries.[48] Thus, a national nosocomial infection control project (NosoLine), supported by the Turkish Hospital Infections Society, has recently started at the Hacettepe University Hospital, Ankara. The project's aim is to develop a regular, standardised surveillance system, allowing electronic data transfer and online announcement of the results to the member centres. To achieve its goals, the problems of gaining financial support and recruiting qualified personnel for data evaluation and processing need to be solved, and additionally all major hospitals will need access to the system.[49]

Despite the absence of extensive data, reports of recent percentages of up to 70% of nosocomial MRSA infections confirm the urgent need for an effective antimicrobial usage policy for our country. To prevent resistant isolates spreading within and between hospitals, proper infection control procedures should be enforced, which currently most hospitals lack. In time we hope to prevent the uncontrolled availability of antimicrobials, increase awareness of such problems to physicians and the community, and have more available funds to support programmes in hospitals.

Conflicts of interest

We declare that we have no conflicts of interest.

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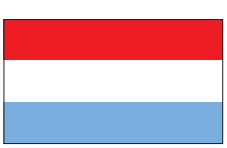

Netherlands

Yes, they do not like to see us coming: physicians, nurses, and hospital administrators may shrink away when the banner of MRSA is raised by the hospital infection-control practitioner—it always means expensive and time-consuming isolation, may mean temporary removal of staff, or the partial or complete locking of wards that have to stop admissions.

Yet the incidence of MRSA in the Netherlands remains one of the lowest of Europe. In 2003, MRSA was isolated from 1601 people, one-fifth of whom were health-care workers, which means that approximately 1280 patients newly acquired MRSA in the course of a year. To put this number into perspective, the Netherlands has 16 million inhabitants, 124 hospitals, and approximately 9 million patient-days of stay in hospital. A timely implementation of a national policy of stringent control measures, and a long-standing tradition in parsimonious antibiotic use surely contributed to keeping MRSA at bay.

As in many other countries, after a short appearance in the late 1960s, MRSA entered the Netherlands in the early to mid-1980s. Three large hospitals in Rotterdam, Amsterdam, and Utrecht experienced outbreaks that were eventually controlled by strict infection-control measures that included isolation of patients, screening of patients and hospital staff members, and closure of wards. Both in Amsterdam and in Utrecht, MRSA was introduced by a patient who had been transferred from a hospital abroad. These early experiences prompted the Dutch Working Party on Infection Prevention (WIP) to formulate national MRSA guidelines. This working group is funded by the Ministry of Health, and its task is to develop guidelines for infection prevention in hospitals, nursing homes and institutions for the mentally handicapped, and dental care and homecare. The guidelines issued by the WIP are considered professional standards and are used as such by the Dutch public health inspector; this undoubtedly contributes to the adherence to the guidelines by nearly all health institutions.

The MRSA guidelines are based on three main principles. First, patients with MRSA are always isolated in single rooms, whether they have an active MRSA infection or not—carriers are also considered potential sources of transmission. Isolation for being a carrier raises anxiety in the patient and their relatives. However, 30% of adults are staphylococcal carriers, and they develop an infection only occasionally, so, in itself, carriage of a staphylococcus that has additional resistance is not a source of worry for the individual patient. Second, patients suspected of potential carriage are always placed in isolation; potential carriage is considered in all patients transferred from hospitals abroad to Dutch hospitals, in patients from Dutch hospitals, or from nursing homes with an actual problem of MRSA, and in patients who have been nursed in the same room as a patient in whom MRSA is detected unexpectedly. This isolation may come

as a shock to people who become ill abroad, are repatriated, and arrive with a sigh of relief in a hospital in the Netherlands, only to be faced with strict isolation measures, where even the family members have to wear gowns and masks upon entering the patient's room. An often-heard reaction is "am I a leper?", and it may be taxing to the attending physician to explain the reasoning behind the precautionary measure. Third, contacts of patients with MRSA—both other patients and hospital staff—are screened for MRSA carriage and treated with mupirocin nasal ointment if found positive. This screening can prove trying for staff, because they are not allowed to return to work unless negative. Fortunately, MRSA is usually quickly lost in normal community life or upon treatment with mupirocin nasal ointment. On occasion, a staff member proves to be a "stubborn" carrier, and several courses of mupirocin and the use of disinfectant soap are needed to clear the carriage. This upsets personal life and the working schedules of staff colleagues, who have to fill in for their colleague during the period he or she is not allowed to work. Fortunately, untreatable carriage is very unusual, but may lead to the necessity to change job. The WIP guidelines for MRSA are also published in English and can be found at http://www.wip.nl.

This very active searching policy implies that many of the MRSA strains that are identified in Dutch hospitals are not actually causing infections, but are merely colonisers at the moment that they are detected. Indeed, of the 1601 strains isolated in the past year, one-fifth were from health-care workers, who very seldom have an active infection when they are screened; the remainder were from patients who may have had an active infection or may just have been colonised.

In the Netherlands, MRSA occurs mainly in isolated cases or in smaller outbreaks, and it is not yet endemic in any hospital. Because of this, it is possible to institute strict control measures whenever needed, although every time they cause great upheaval in the implicated ward, which has to isolate patients and screen patients and staff. The decreased therapeutic options, the nightmare of impending vancomycin resistance, and the higher numbers of therapeutic failures that accompany infections with MRSA provide a firm ground for the Dutch policy. It is therefore strongly supported by the Inspectorate of Health Care and by all microbiologists, infectious disease specialists, and infection-control officers involved.

There is the odd dissenting voice of a surgeon or intensive-care physician who points to his colleagues in the UK or the USA where MRSA is rampant—"medical life is possible over there isn't it?" Part of the unease of physicians is the result of misunderstandings and some "urban myths"—more appropriately "hospital myths"—about MRSA. For instance, surgeons may think that they cannot operate on a patient who carries MRSA. Nothing could be further from the truth. Yes, elective surgery might be postponed, but all necessary surgery should go on as planned, with extra precautions. Again, it is too often forgotten that 30% of all adults are staphylococcus carriers, and that the carriage in itself does no harm.

Up to now there have been neither legal nor ethical qualms about the Dutch "search, isolate, and destroy" strategy, as in the end, all sections of medical life in the Netherlands—physicians, nurses, and administrators—see the value of prevention. After careful explanation, even if some measures may tax the ingenuity of administrators and staff, the experience is almost invariably one of excellent cooperation, and most people involved enjoy the process of working for the greater good.

Conflicts of interest
I declare that I have no conflicts of interest.

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MRSA is everybody's business

Although the exact burden of disease caused by MRSA remains largely unknown, most experts would agree that MRSA infections represent an important clinical and public-health problem. We hardly need to call readers' attention to the thousands of articles published over the past three decades about epidemiological and microbiological aspects of MRSA. Yet uncertainty remains about the best approach to prevent and control this worldwide plague.

In this issue of *The Lancet Infectious Diseases*, several authors offer insight into MRSA control approaches used in different areas of the world. Countries like Finland, Denmark, and the Netherlands have managed to keep MRSA at a low level using surveillance cultures of patients and personnel, strictly enforced contact precautions, and judicious use of broad-spectrum antibiotics. Unfortunately, these countries are facing now the paradoxical situation that transmission of community-acquired MRSA may jeopardise their well-established strategies to control nosocomial MRSA. Denmark, for instance, has seen a substantial increase in MRSA since 2003, due to the epidemic spread of genetically distinct community-acquired MRSA strains.[50] Conversely, many middle-income countries (eg, Turkey, Argentina) and some high-income countries (eg, Italy, Greece, UK, USA) that were not able to install stringent counter-measures now have hyper-endemic MRSA and are obliged to concentrate available resources to prevent MRSA infections in high-risk populations—eg, dialysis, transplant, or critically ill patients. A few countries with endemic MRSA (eg, Australia, France, Belgium) have managed to stabilise or even decrease MRSA prevalence in confined geographic areas. On the other hand, several Asian countries (eg,

China, South Korea, Japan) have more or less ignored this public-health problem for a long time, resulting in some of the highest MRSA incidence rates worldwide. In these countries, financial incentives for physicians' antibiotic prescribing linked to the pharmaceutical reimbursement system have strongly influenced antibiotic overuse and increased antibiotic selection pressure on MRSA; an issue that has only recently been adequately addressed at the policy level.

Why do MRSA rates vary so much across countries? Differences are caused largely by uneven control and isolation measures, hand hygiene practices, antibiotic prescribing behaviours, and allocation of resources.[51] Cultural and economic factors pervade all aspects of MRSA control, which can only be fully successful if strict measures and policies are installed at an early stage of MRSA dissemination, sufficiently supported by financial and staff resources. Especially at the early phase of a nationwide MRSA epidemic, the full clinical impact of MRSA may not be visible, leading to misconceptions among clinicians and policy makers that MRSA may not be a threat to patient safety.

Do we have any hope for the future? As MRSA surveillance systems and control strategies improve in quality and become more coherent among different countries, international pressure may start to be applied to induce change in countries where infection-control policies are lax or non-existent. The situation with MRSA might become comparable to that observed for other infectious problems such as severe acute respiratory syndrome and mad cow disease—economic and political pressure may contribute to compliance and uniformity in control measures and to allocation of resources to improve patient safety.[52] Yet stringent MRSA control worldwide will remain difficult to implement and will require intensive surveillance efforts and substantial resources. To achieve this goal may be possible, as shown by several examples where successful action against MRSA has been endorsed by strong policy support.

Adequate hand hygiene decreases the transmission of MRSA, although the practice is difficult to enforce, because of psychological, practical, and organisational barriers. Promoting hand hygiene to improve patient safety and decrease health-care-associated infections worldwide constitutes a core component of the first Global Patient Safety Challenge ("Clean Care is Safer Care") of the WHO World Alliance for Patient Safety launched in 2004. If successful, Clean Care is Safer Care will certainly have a positive impact on MRSA transmission and other antibiotic-resistant infections.

See http://www.who.int/patientsafety/en/

Low MRSA prevalence in a country is good news in that preventive measures are more likely to succeed than if endemic MRSA levels are already present. Unfortunately, for key questions regarding the most cost-effective control of endemic MRSA, we have only weak or contradicting evidence. Several well-conducted studies from France, Germany, the UK, and the USA have recently illustrated this dilemma.[53–57] Whatever the final outcome of this ongoing debate, health authorities and policy makers are well-advised to put effort and money into their MRSA control efforts. MRSA is everybody's business, not only that of hospital epidemiologists and a few opinion leaders.

Conflicts of interest

We declare that we have no conflicts of interest.

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References

1 National Nosocomial Infections Surveillance System. National Nosocomial Infections Surveillance (NNIS) System Report, data summary from January 1992 through June 2004, issued October 2004. *Am J Infect Control* 2004; **32:** 470–85.

2 Roghmann MC. Predicting methicillin resistance and the effect of inadequate empiric therapy on survival in patients with *Staphylococcus aureus* bacteremia. *Arch Intern Med* 2000; **160:** 1001–04.

3 Biedenback DJ, Moet GJ, Jones RN. Occurrence and antimicrobial resistance pattern comparisons among bloodstream infection isolates from the SENTRY Antimicrobial Surveillance Program (1997–2002). *Diagn Microbiol Infect Dis* 2004; **50:** 59–69.

4 Lodise TP, McKinnon PS, Swiderski L, Rybak MJ. Outcomes analysis of delayed antibiotic treatment for hospital-acquired *Staphylococcus aureus* bacteremia. *Clin Infect Dis* 2003; **36:** 1418–23.

5 Cosgrove SE, Qi Y, Kaye KS, Harbarth S, Karchmer AW, Carmeli Y. The impact of methicillin resistance in *Staphylococcus aureus* bacteremia on patient outcomes: mortality, length of stay, and hospital charges. *Infect Control Hosp Epidemiol* 2005; **26:** 166–74.

6 Engemann JJ, Carmeli Y, Cosgrove SE, et al. Adverse clinical and economic outcomes attributable to methicillin resistance among patients with *Staphylococcus aureus* surgical site infection. *Clin Infect Dis* 2003; **36:** 592–98.

7 Manian FA, Meyer PL, Setzer J, Senkel D. Surgical site infections associated with methicillin-resistant *Staphylococcus aureus*: do postoperative factors play a role? *Clin Infect Dis* 2003; **36:** 863–68.

8 Fridkin SK, Hageman J, McDougal LK, et al. Epidemiological and microbiological characterization of infections caused by *Staphylococcus aureus* with reduced susceptibility to vancomycin, United States, 1997–2001. *Clin Infect Dis* 2003; **36:** 429–39.

9 Tenover FC, McDonald LC. Vancomycin-resistant staphylococci and enterococci: epidemiology and control. *Curr Opin Infect Dis* 2005; **18:** 300–05.

10 Sakoulas G, Moise-Broder PA, Schentag J, Forrest A, Moellering RC Jr, Eliopoulos GM. Relationship of MIC and bactericidal activity to efficacy of vancomycin for treatment of methicillin-resistant *Staphylococcus aureus* bacteremia. *J Clin Microbiol* 2004; **42:** 2398–402.

11 Fowler VG Jr, Sakoulas G, McIntyre LM, et al. Persistent bacteremia due to methicillin-resistant *Staphylococcus aureus* infection is associated with agr dysfunction and low-level in vitro resistance to thrombin-induced platelet microbicidal protein. *J Infect Dis* 2004; **190:** 1140–49.

12 Kollef MH, Rello J, Cammarata SK, Croos-Dabrera RV, Wunderink RG. Clinical cure and survival in Gram-positive ventilator-associated pneumonia: retrospective analysis of two double-blind studies comparing linezolid with vancomycin. *Intensive Care Med* 2004; **30:** 388–94.

13 Herold BC, Immergluck LC, Maranan MC, et al. Community-acquired methicillin-resistant *Staphylococcus aureus* in children with no identified predisposing risk. *JAMA* 1998; **279:** 593–98.

14 Seal JB, Moreira B, Bethel CD, Daum RS. Antimicrobial resistance in *Staphylococcus aureus* at the University of Chicago Hospitals: a 15-year longitudinal assessment in a large university-based hospital. *Infect Control Hosp Epidemiol* 2003; **24:** 392–96.

15 Weber JT. Community-associated methicillin-resistant *Staphylococcus aureus*. *Clin Infect Dis* 2005; **41:** S269–72.

16 Kaplan SL, Hulten KG, Gonzalez BE, et al. Three-year surveillance of community-acquired-*Staphylococcus aureus* infections in children. *Clin Infect Dis* 2005; **40:** 1785–91.

17 Kazakova SV, Hageman JC, Matava M, et al. A clone of methicillin-resistant *Staphylococcus aureus* among professional football players. *N Engl J Med* 2005; **352:** 468–75.

18 Daum RS, Ito T, Hiramatsu K, et al. A novel methicillin-resistance cassette in community-acquired methicillin-resistant *Staphylococcus aureus* isolates of diverse genetic backgrounds. *J Infect Dis* 2002; **186:** 1344–47.

19 Lewis JS, Jorgensen JH. Inducible clindamycin resistance in staphylococci: should clinicians and microbiologists be concerned? *Clin Infect Dis* 2005; **40:** 280–85.

20 Muto CA, Jernigan JA, Ostrowsky BE, et al. SHEA guideline for preventing nosocomial transmission of multidrug-resistant strains of *Staphylococcus aureus* and enterococcus. *Infect Control Hosp Epidemiol* 2003; **24:** 362–86.

21 Lucet JC, Chevret S, Durand-Zaleski I, Chastang C, Regnier B, Multicenter Study Group. Prevalence and risk factors for carriage of methicillin-resistant *Staphylococcus aureus* at admission to the intensive care unit: results of a multicenter study. *Arch Intern Med* 2003; **163:** 181–88.

22 Lucet JC, Paoletti X, Lolom I, et al. Successful long-term program for controlling methicillin-resistant *Staphylococcus aureus* in intensive care units. *Intensive Care Med* 2005; **31:** 1051–57.

23 Sunenshine RH, Liedtke LA, Fridkin SK, Strausbaugh LJ, Infectious Diseases Society of America Emerging Infections Network. Management of inpatients colonized or infected with antimicrobial-resistant bacteria in hospitals in the United States. *Infect Control Hosp Epidemiol* 2005; **26:** 138–43.

24 Nijssen S, Bonten MJ, Weinstein RA. Are active microbiological surveillance and subsequent isolation needed to prevent the spread of methicillin-resistant *Staphylococcus aureus*? *Clin Infect Dis* 2005; **40:** 405–09.

25 Murchan S, Kaufmann P, Deplano A, et al. Harmonisation of pulsed-field gel electrophoresis for epidemiological typing of methicillin-resistant *Staphylococcus aureus* by consensus in European laboratories and its application for tracing the spread of related strains. *J Clin Microbiol* 2003; **41:** 1574–85.

26 Cookson B. Methicillin-resistant *Staphylococcus aureus*: a modern epidemic. *Evidence-Based Healthcare and Public Health* 2005; **9:** 1–3.

27 Cooper BS, Stone SP, Kibbler CC, et al. Systematic review of isolation policies in the hospital management of methicillin-resistant *Staphylococcus aureus*: a review of the literature with epidemiological and economic modelling. *Health Technol Assess* 2003; **7:** 39.

28 Ayliffe GAJ, Buckles A, Casewell MW, et al. Revised guidelines for the control of methicillin resistant *Staphylococcus aureus* infections in hospitals. *J Hosp Infect* 1998; **39:** 253–90.

29 Pittet D, Safran E, Harbarth S, et al. Automatic alerts for methicillin-resistant *Staphylococcus aureus* surveillance and control: role of a hospital information system. *Infect Control Hosp Epidemiol* 1996; **17:** 496–502.

30 Naimi TS, LeDell KH, Como-Sabetti K, et al. Comparison of community- and health care-associated methicillin-resistant *Staphylococcus aureus* infection. *JAMA* 2003; **290:** 2976–84.

31 Hisata K, Kuwahara-Arai K, Yamanoto M, et al. Dissemination of Meticillin-resistant staphylococci among healthy Japanese children. *J Clin Microbiol* 2005; **43:** 3364–72.

32 Hiramatsu K, Hanaki H, Ino T, Yabuta K, Oguri T, Tenover FC. meticillin-resistant *Staphylococcus aureus* clinical strain with reduced vancomycin susceptibility. *J Antimicrob Chemother* 1997; **40:** 135–36.

33 Hiramatsu K, Aritaka N, Hanaki H, et al. Dissemination in Japanese hospitals of strains of *Staphylococcus aureus* heterogeneously resistant to vancomycin. *Lancet* 1997; **350:** 1670–73.

34 Kansanterveyslaitos Folkhalsoinstitutet (National Public Health Institute). Ohje metisilliniresistenttien *Staphylococcus aureusten* torjunnasta. http://www.ktl.fi/attachments/suomi/osastot/infe/julkaisut/mrsa2004.pdf (accessed Sept 6, 2005).

35 Salmenlinna S, Lyytikäinen O, Vuopio-Varkila J. Community-acquired methicillin-resistant *Staphylococcus aureus*, Finland. *Emerging Infect Dis* 2002, **8:** 602–07.

36 Kerttula AM, Lyytikäinen O, Salmenlinna S, Vuopio-Varkila J. Changing epidemiology of methicillin-resistant *Staphylococcus aureus* in Finland. *J Hosp Infection* 2004, **58:** 109–14.

37 Sieradzki K, Tomasz A. Suppression of β-lactam antibiotic resistance in a meticillin-resistant *Staphylococcus aureus* through synergic action of early cell wall inhibitors and some other antibiotics. *J Antimicrob Chemother* 1997; **39** (suppl A)**:** 47–51.

38 Kocagöz S, Gür D, Uzun Ö, Akova M. Resistance to meticillin of Staphylococcus in Turkey. 8th Turkish Microbiology and Infectious Diseases Congress; Antalya, Turkey; Oct 6–7, 1997. Abstract 776.

39 Akata F. Prevelance of resistant Gram-positive infections. *Antibiyotik ve Kemoterapi Dernegi Dergisi* 2001; **15:** 391–406 (in Turkish).

40 Sacilik SC, Kisa O, Basustaoglu A, Cokmus C. Protein profiles and prevalence of meticillin resistant *Staphylococcus aureus* (MRSA) in Gülhane Military Academy Hospital in Turkey. *Turk J Biol* 2000; **24:** 809–16.

41 Oncul O, Yuksel F, Altunay H, Acikel C, Celikoz B, Cavuslu S. The evaluation of nosocomial infection during 1-year-period in the burn unit of a training hospital in Istanbul, Turkey. *Burns* 2002; **28:** 738–44.

42 Tunger O, Ozbakkaloglu B, Aksoy H. Trends in antimicrobial resistant staphylococci in an university hospital over a 6-year period. *Int J Antimicrob Agents* 2001; **18:** 93–96.

43 Erbay H, Yalcin AN, Serin S, et al. Nosocomial infections in intensive care unit in a Turkish university hospital: a 2-year survey. *Intensive Care Med* 2003; **29:** 1482–88.

44 Murray BE. New aspects of antimicrobial resistance and the resultings therapeutic dilemmas. *J Infect Dis* 1991; **163:** 1185–94.

45 Vannuffel P, Gigi J, Ezzedine H, et al. Specific detection of meticillin-resistant staphylococcus species by multiplex PCR. *J Clin Microbiol* 1995; **33:** 2864–67.

46 Öztop AY, Pinarbasi H, Kocagöz S, Bakirci MZ. Molecular genotyping of meticillin-resistant *Staphylococcus aureus* strains in a teaching hospital in Turkey. *Microb Drug Resist* 2004; **10:** 154–59.

47 De Lencastre H, Severina EP, Roberts RB, et al. Testing the efficacy of a molecular surveillance network: meticillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant *Enterococcus faecium* (VREF) genotypes in six hospitals in the metropolitan New York city area. *Microb Drug Resist* 1996; **2:** 343–51.

48 Yalcin AN. Socioeconomic burden of nosocomial infections. *Indian J Med Sci* 2003; **57:** 450–56.

49 Ünal S. Hospital infections: where are we? *Hastane Infeksiyonlari Dergisi* 2004; **8:** 129–31 (in Turkish).

50 Faria NA, Oliveira DC, Westh H, et al. Epidemiology of emerging methicillin-resistant *Staphylococcus aureus* (MRSA) in Denmark: a nationwide study in a country with low prevalence of MRSA infection. *J Clin Microbiol* 2005; **43:** 1836–42.

51 Harbarth S, Albrich W, Goldmann DA, Huebner J. Control of multiply resistant cocci: do international comparisons help? *Lancet Infect Dis* 2001; **1:** 251–61.

52 Harbarth S, Samore MH. Antimicrobial resistance determinants and future control. *Emerg Infect Dis* 2005; **11:** 794–801.

53 Cepeda JA, Whitehouse T, Cooper B, et al. Isolation of patients in single rooms or cohorts to reduce spread of MRSA in intensive-care units: prospective two-centre study. *Lancet* 2005; **365:** 295–304.

54 Biant LC, Teare EL, Williams WW, Tuite JD. Eradication of methicillin resistant *Staphylococcus aureus* by "ring fencing" of elective orthopaedic beds. *BMJ* 2004; **329:** 149–51.

55 Nijssen S, Bonten MJ, Weinstein RA. Are active microbiological surveillance and subsequent isolation needed to prevent the spread of methicillin-resistant *Staphylococcus aureus*? *Clin Infect Dis* 2005; **40:** 405–09.

56 Wernitz MH, Swidsinski S, Weist K, et al. Effectiveness of a hospital-wide selective screening programme for methicillin-resistant *Staphylococcus aureus* (MRSA) carriers at hospital admission to prevent hospital-acquired MRSA infections. *Clin Microbiol Infect* 2005; **11:** 457–65.

57 Lucet JC, Paoletti X, Lolom I, et al. Successful long-term program for controlling methicillin-resistant *Staphylococcus aureus* in intensive care units. *Intensive Care Med* 2005; **31:** 1051–57.