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Infection control programmes to control antimicrobial resistance

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World Health Organization

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A BACKGROUND DOCUMENT FOR
THE WHO GLOBAL STRATEGY
FOR CONTAINMENT OF
ANTIMICROBIAL
RESISTANCE

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Executive Summary

1. Health care facilities, particularly acute care facilities, are important sites for the development of antimicrobial resistance. The intensity of antimicrobial use together with populations highly susceptible to infection create an environment which facilitates both the emergence and transmission of resistant organisms.
2. Optimal infection control programmes in health care facilities decrease the frequency of nosocomial infection. Such programmes have been identified as important components of any comprehensive strategy for the control of antimicrobial resistance, primarily through limiting transmission of resistant organisms among patients. The successful containment of antimicrobial resistance in acute care facilities, however, also requires adequate clinical microbiology laboratory support and a strong antimicrobial use programme.
3. Infection control interventions are effective in controlling some outbreaks of colonization and infection with antimicrobial-resistant organisms in health care facilities. In fact, antimicrobial resistance frequently is a phenotypic marker for the outbreak organism which facilitates identification and early initiation of interventions to control the outbreak. The application of infection control measures, however, is not uniformly successful in limiting outbreaks with resistant organisms.
4. Barrier practices including patient isolation and the use of gloves, gowns, or masks, are widely recommended for the control of endemic antimicrobial resistance. The effectiveness of these practices is controversial, and studies evaluating their efficacy are contradictory. The extent to which these practices decrease resistance likely varies with other determinants, such as prevalence of antimicrobial-resistant organisms in the facility, characteristics of the patient population, staffing ratio and expertise, and patient volumes. New implementation of these practices, especially in high-risk units, decreases transmission of some resistant organisms. Barrier practices cannot, however, by themselves, fully prevent nor ultimately contain the progression of resistance.
5. The current worldwide epidemics of MRSA and VRE have progressed despite intense national and local infection control measures to identify and contain the spread of these organisms.
6. The appropriate use of prophylactic antimicrobials prevents some nosocomial infections. However, any prophylactic antimicrobial use, especially in high-risk patients, contributes to antimicrobial pressure and to the emergence of antimicrobial-resistant organisms. In this case, appropriate infection control activity may actually promote antimicrobial resistance.
7. In some facilities, reallocation of infection control resources to comply with recommendations for control of colonization of MRSA and VRE has compromised other infection control functions, potentially increasing the frequency of nosocomial infection.
8. Overall, infection control programmes have some efficacy in containing antimicrobial resistance, particularly when an outbreak with a resistant strain is identified. Other infection control practices decrease transmission of both resistant and susceptible organisms among patients, and intensification of these practices to limit transmission of resistant organisms likely has some short-term efficacy in decreasing endemic resistance. Ultimately, however, limiting antimicrobial resistance rests primarily with antimicrobial use rather than infection control.
9. If the infection control responsibility is expanded to incorporate control of transmission and colonization with resistant organisms, rather than decreasing infections, additional resources to support the increased activity must be allocated.

10. Further systematic evaluation of infection control interventions in containing endemic antimicrobial resistance in acute care facilities, as well as other health care settings, is needed. This should include studies of the natural history and impacts of antimicrobial-resistant organisms in facilities as well as effectiveness, feasibility, and costs of specific infection control interventions.

1. Antimicrobial resistance in health care facilities

Antimicrobial resistance is a predictable outcome of antimicrobial use. The rapidity with which resistance emerges and its extent are proportional to the intensity of antimicrobial use (1). Resistance first emerges in populations with a high frequency of infection, due to either underlying patient status or interventions compromising host defences, resulting in a high rate of antimicrobial use. Where patients at risk are in close proximity, the transmission of organisms between patients will be facilitated, and the opportunity for a single strain to disseminate widely is enhanced. All these features are present in health care facilities, particularly acute care facilities and areas such as intensive care units (2). Thus, health care facilities, particularly those which are large and care for the most complex patients, are a focal point in the emergence of antimicrobial resistance.

Resistant organisms have repeatedly been first described in high-risk patients of acute care facilities (Table I). Some organisms, such as resistant fungi in neutropenic patients (3), or resistant *Pseudomonas aeruginosa* in intensive care unit patients (4), are a risk only for selected hospitalized patients. These organisms contribute to morbidity and cost in restricted patient groups, with little impact in less immunocompromised hospitalized patients or in the community. In other instances, such as extended spectrum β -lactamase producing Enterobacteriaceae (5) or vancomycin-resistant enterococci (6), strains spread among patients and may cause infection in patients with less acuity in the acute care hospital, in chronic care or long-term care facilities, or in community health care. An organism of particular concern is *Staphylococcus aureus*, an important human pathogen in both the hospital and the community. Resistance, first to penicillin in the 1950s (7), and now methicillin (8), has emerged and became widespread in hospitals and subsequently spread to the community. In another example, hospitals were found to be the source of strains of resistant *Salmonella* which caused com-

munity infections in Brazil (9). The flow of resistant organisms is not, however, unidirectional. Resistant strains have emerged in the community, such as penicillin-resistant *Streptococcus pneumoniae* (10) and resistant *Salmonella* spp (11,12), and been introduced into acute care facilities with resulting nosocomial infections.

TABLE I. **ANTIMICROBIAL-RESISTANT ORGANISMS OF CONCERN IN HEALTH CARE FACILITIES**

Organism	Resistant to
<i>Staphylococcus aureus</i>	methicillin vancomycin
<i>Staphylococcus epidermidis</i>	vancomycin
Enterococci	aminoglycoside (high level) ampicillin vancomycin
<i>Streptococcus pneumoniae</i>	penicillin
Enterobacteriaceae	aminoglycosides third-generation cephalosporins monobactams ceftazidime
<i>Pseudomonas aeruginosa</i>	fluoroquinolones extended-spectrum penicillins fluoroquinolones aminoglycosides ceftazidime carbapenems
<i>Acinetobacter</i> spp	aminoglycosides ceftazidime carbapenems
<i>Mycobacterium tuberculosis</i>	isoniazid rifampin streptomycin ethambutol pyrazinamide
<i>Candida</i> spp	amphotericin b azoles
<i>Herpes simplex</i>	acyclovir
Cytomegalovirus	foscarnet

2. Containing antimicrobial resistance in health care facilities

Multifaceted proposals to address the problem of antimicrobial resistance have uniformly stated that optimal infection control programmes in health care facilities are an essential component. The WHO Global Strategy for Containment of Antimicrobial Resistance recommends that hospital management “establish infection control programmes with responsibility for effective management of antimicrobial resistance in hospitals and ensure that all hospitals have access to such a programme” (1). Recommendations for strengthening infection control programmes and activity are also included in the United States Public Health Action Plan to Combat Antimicrobial Resistance (13), in *Controlling Antimicrobial Resistance: An Integrated Action Plan for Canadians* (14), and the European Commission Opinion of the Scientific Steering Committee on Antimicrobial Resistance (15). Despite this consensus on the importance of infection control activities in health care facilities, there has been limited evaluation of the evidence to support the effectiveness of infection control in containing antimicrobial resistance and preventing adverse clinical outcomes attributable to antimicrobial resistance.

This discussion will review the evidence supporting the efficacy of infection control programmes and activities in containing the prevalence of antimicrobial resistance and limiting infections with resistant organisms acquired in health care facilities. The question to be addressed is what, if any, is the additional benefit of an infection control programme in the containment of antibiotic resistance beyond the benefit inherent in overall infection

prevention. This will include discussion of specific components of infection control activity, and will focus primarily on acute care facilities. Important questions requiring further investigation to clarify and quantify the impact of effective infection control strategies in containing antimicrobial resistance will also be identified.

In health care facilities, the infection control programme is one of three essential overlapping programmes with activities which address the problem of antimicrobial resistance (1,2). The clinical microbiology laboratory provides isolation and susceptibility testing of organisms from clinical specimens, and surveillance data to summarize the prevalence of antimicrobial resistance in a facility. The third essential activity is the antimicrobial use programme which makes recommendations for antimicrobials for the hospital formulary considering the impacts of antimicrobial resistance both for the individual infected patient as well as the environment, and monitors antimicrobial use and appropriateness. These three programmes must function cooperatively to support the goal of containment of antimicrobial resistance, but also have responsibility for service delivery beyond antimicrobial resistance. While acknowledging that integration of infection control, the laboratory, and antimicrobial use programmes are essential to address antimicrobial resistance, this discussion will focus specifically on the infection control programme. Activities of the other two programmes will only be addressed where they are directly relevant to infection control functions.

3. Infection control programmes

3.1 Effectiveness of infection control programmes

The essential features and appropriate resources for an optimal infection control programme have been identified (16) (Table II). The SENIC study showed that effective infection control programmes which included surveillance, control activities, and appropriate personnel and leadership decreased the frequency of endemic nosocomial infections by 30% to 50% (17). The specific role of such programmes in containing antimicrobial resistance has not been reported. An assumption would be that such a programme would decrease antimicrobial-resistant infections proportional to the overall decrease in nosocomial infections. The absolute number of infections with resistant organisms would, then, decrease but the proportionate amount of antimicrobial-resistant infections would remain stable.

TABLE II. ACTIVITIES OF AN OPTIMAL INFECTION CONTROL PROGRAMME

— surveillance of nosocomial infections
— outbreak investigation and control
— policy development, review and compliance monitoring
isolation practices
hand hygiene
sterilization/disinfection of equipment and supplies
housekeeping
laundry
food
— employee health relevant to infections
— education of staff, patients, visitors

3.2 Impact on antimicrobial resistance

The impact of infection control on antimicrobial-resistant infections, however, is not necessarily straightforward. If the overall frequency of infection in a facility is decreased, then antimicrobial use may also be decreased. This would mean less antimicrobial pressure in the institutional environment, leading to a decrease in the prevalence of antimicrobial-resistant organisms and proportionately fewer infections with resistant organisms with intensified infection control activity. However, in-

fections least likely to be preventable through infection control activity are those which occur in the most highly immunocompromised patients, where patient vulnerability overwhelms preventive efforts. Such patients would include, for example, those receiving allogeneic bone marrow transplants or with over 50% body surface area burns. These are also the patients most likely to require prophylactic or therapeutic antimicrobials. Thus, infection control programmes may be less effective in decreasing infections for these patients at greatest risk for antimicrobial-resistant organisms. With intensification of infection control activity, the proportion of antimicrobial-resistant infections may, then, increase.

The goal of infection control programmes is to decrease the incidence of infections in patients and staff (16). Considerations relevant to antimicrobial-resistant organisms, however, extend beyond this goal by including patient colonization with resistant organisms as well as infection. The outcome of colonization is seen to be an important measure of the total burden of antimicrobial resistance in a population, as well as predicting the future burden of infection with these organisms. The effectiveness of an optimal infection control programme in decreasing the total burden of colonization of patients with resistant organisms has also not been adequately evaluated.

3.3 Impact on MRSA and VRE

While the overall impact on antimicrobial-resistant organisms in a facility is not known, some observations relevant to specific organisms have been reported. For methicillin-resistant *Staphylococcus aureus* (MRSA), intense and comprehensive infection control programmes, including screening of staff and patients, strict isolation or cohorting, and decolonization therapy of patients and staff were initially recommended for control in some countries. These interventions are both expensive and burdensome. In both the United States (18, 19) and the United Kingdom (20, 21), and elsewhere (22)

recommendations have subsequently been adjusted to promote less intense infection control measures. This followed from an apparent failure of the initial recommendations to limit the increase in endemic MRSA (22, 23), and repeated reports where decreased intensity of infection control interventions was not followed by increased rates of nosocomial transmission or infection with MRSA in the facility (24–28).

A relevant report with a unique perspective is that by Meers and Leong (29). They describe an experience with MRSA in a newly opened teaching hospital where no infection control programme to control MRSA was ever implemented. The organism was first isolated in patient specimens shortly after the hospital opened, and the prevalence of MRSA in *S. aureus* isolates increased over the next year. For the subsequent three years the prevalence of MRSA remained stable, and was responsible for about 50% of nosocomial *S. aureus* infections. The authors argue the nosocomial *S. aureus* infection rate was similar to that reported from other facilities, and the only negative impact of MRSA in the facility was the increased cost of antimicrobials to treat infected patients. They suggest their experience did not support intense and costly infection control interventions to control endemic MRSA in an acute care facility.

Similar to the MRSA experience, the recommendation for and widespread implementation of

comprehensive guidelines to control endemic vancomycin-resistant enterococci (VRE), including intense infection control interventions (30), have not prevented progression of the American VRE epidemic nationally (31), or in individual institutions (32–36). Whether these intense infection control programmes delayed the progression of endemicity with these organisms cannot be assessed.

3.4 Summary

Overall, while optimal infection control programmes should be expected to decrease the occurrence of infections and, possibly, colonization with resistant organisms, the effect of such programmes and the duration of any effect are not known. In fact, the efficacy of an infection control programme in limiting endemic colonization or infection with resistant organisms has not been unequivocally demonstrated. The available evidence, primarily the experience with MRSA and VRE, suggests infection control programmes have limited efficacy in preventing endemic infection or colonization with antimicrobial-resistant organisms becoming established in a facility. If programmes do decrease the prevalence of resistance, the duration of this effect, especially in the face of an increasing prevalence of resistant organisms in other facilities or in the community is also unclear (37, 38).

4. Outbreak management

4.1 Elements of outbreak management

Effective outbreak management is an essential function of an infection control programme (16). Specific activities include identification, coordination of response, case-finding, description of the extent and temporal course, input into case management, analysis of exposure and patient variables to identify risks, and introduction and evaluation of specific control measures to terminate the outbreak. Mobilization of resources beyond infection control is usually necessary, and the clinical microbiology laboratory and antimicrobial use programme are two key components. In outbreak control the activities of these two programmes are an integral part of the infection control response.

4.2 Literature review

The largest body of evidence which supports a specific role for infection control in containing antimicrobial resistance is in outbreak control. Many reports which describe hospital outbreaks of antimicrobial-resistant organisms are summarized in the annex to this report. These were identified through a Medline search using the key words outbreak and resistant, supplemented by complete review of infection control journals—the *Journal of Hospital Infection*, *Infection Control and Hospital Epidemiology*, and the *American Journal of Infection Control*. Only reports in English and those published after 1970 have been included. The focus is largely acute care facilities, and only includes those reports where sufficient information was provided to assess the impact of control measures. The interventions instituted, as far as could be ascertained from information in the published reports, are also summarized.

4.3 Limitations of published reports

In evaluating this body of information, it must be appreciated there is likely substantial publication bias. Outbreaks are more likely to be reported if they have occurred in an academic centre where

publication is encouraged, or if there is something unique about the outbreak. This might include an outbreak with a new strain, such as an antimicrobial-resistant organism, identification of a vector not previously described, or the use of a new epidemiological typing method. Outbreaks successfully controlled are also more likely to be reported than those for which control measures were not effective, or were only partially effective.

Another limitation in assessing the effectiveness of outbreak investigation and control measures is that reports are descriptive rather than comparative. Interventions are applied universally within the outbreak population and there is no control group, randomization, or blinded assessment. This introduces bias in evaluating the effectiveness of the interventions. There are obvious reasons for these limitations, including ethical considerations and the need for immediate and complete containment, but the potential bias must be recognized. With no control population, apparent containment of the outbreak may simply reflect the natural history of the outbreak strain in the population (39). In addition, the impact of any single intervention can seldom be ascertained as multiple, usually simultaneous, interventions are invariably initiated. Many reports also provide a limited duration of follow-up, and where control or eradication is reported, the durability of the effect is not known.

One example illustrating the difficulty in evaluating the contribution of outbreak control in containment is the report of Bernards et al. (40). This describes three patients transferred to three different Dutch hospitals who were colonized or infected with both MRSA and antimicrobial-resistant *Acinetobacter baumannii*. All patients were immediately placed in strict isolation, following Dutch infection control guidelines. There was no transmission of MRSA in any facility. Two of the three facilities experienced outbreaks with the imported *Acinetobacter* strains—in one facility the outbreak resolved spontaneously with no investigation or control measures, and in the other facility the strain was eradicated after intense outbreak investigation

and control. The authors report the one facility which did not experience an outbreak was the only one with isolation facilities appropriate to prevent airborne spread, and suggests this explains the absence of transmission in that facility. However, measures for the control of airborne transmission were not instituted for at least one of the two outbreaks, and this resolved. From this report, it is possible to conclude that isolation precautions are effective, or that they are ineffective, that outbreak control is necessary and effective, or is not necessary, and that respiratory isolation is essential, or it is not necessary!

4.4 Control of outbreaks caused by resistant organisms

Even given these limitations, a summary assessment of the reports in the annex would be that outbreak management is effective in limiting the spread of and preventing infections caused by antimicrobial-resistant organisms in the acute care hospital. Many of these outbreaks were, in fact, identified because the outbreak strain had a unique antimicrobial susceptibility. They may not have been recognized or controlled as promptly if the organisms were not phenotypically unique because of the resistance marker. The effectiveness of interventions is most convincing for those outbreaks where a unique environmental reservoir or staff member who was a carrier were identified and there was abrupt and complete termination of transmission with eradication of the reservoir. The many reports describing eradication of a new MRSA strain from an institution without endemic MRSA are also convincing evidence for the effectiveness of outbreak management. Finally, repeated reports of termination of multiply-resistant tuberculosis outbreaks among hospitalized HIV patients and staff following the introduction of interventions to control airborne transmission document that appropriate infection control interventions are effective for containing outbreaks with this organism.

Despite this assessment, a theme emerging from many reports is that initial interventions were not

effective. These initial interventions usually included intensification of hand hygiene, barrier precautions or isolation, and staff education, all of which would be reinforcing usual infection control practice. Further control measures introduced after failure of these initial interventions usually included extraordinary measures, such as cohorting of patients and staff, ward closure, treatment of colonization of patients or staff, or antimicrobial restriction. These practices would not normally be sustained once the outbreak is contained. In many reports, interventions decreased the frequency of infection or colonization, but could not eradicate the strain. In some reports, despite intense, multi-faceted control interventions, the outbreak was not contained, and the outbreak strain became endemic in the institution.

4.5 Spontaneous disappearance of resistant strains

Several reports also describe the emergence, dissemination, and subsequent spontaneous decrease or disappearance of an outbreak strain in the absence of control efforts. The disappearance of certain MRSA phage types from Europe in the 1970s and 1980s may be one example (41, 42). Spontaneous decline or disappearance has also been reported in American facilities for gentamicin-resistant Enterobacteriaceae (43, 44) and *Pseudomonas aeruginosa* (45), and even aminoglycoside-resistant transmissible elements (46). In some reports, an apparent environmental reservoir was eliminated without specific control interventions (47–49). Factors which explain the apparently spontaneous decline or disappearance of resistant strains are not known. An important variable, of course, is antimicrobial practice. The natural history of dissemination, persistence, and replacement of antimicrobial-resistant strains requires further study. These observations of apparently spontaneous resolution or decline in resistant organisms causing outbreaks, however, suggests the impact of control measures may be overestimated in some reports.

5. Handwashing/hand hygiene

5.1 Recommendations

Many antimicrobial-resistant organisms, including MRSA and VRE, are primarily transmitted between patients on the hands of staff. Appropriate hand decontamination should be effective in decreasing the transmission of these organisms, as well as strains that are not antimicrobial-resistant. There would not, however, be any unique benefit for resistant organisms. Good practice will limit transmission of all organisms carried on the hands of staff, and some of these will be antimicrobial-resistant.

Hand decontamination for staff of health care facilities participating in direct patient care may be with soap and water, or an antiseptic or antimicrobial solution. Handwashing is effective in preventing nosocomial infections (50), as first demonstrated by the classic studies of Semmelweis (51). The evidence to support specific practices in hand decontamination, however, including frequency, products, and methods is limited as reports are generally non-comparative, observational, or comprised of *in vitro* studies. The recently published evidence-based “Guidelines for Preventing Hospital-acquired Infections” from the United Kingdom documents this when seven recommendations for hand hygiene are made, all with a level of evidence of category 3—expert opinion with limited scientific evidence (52). Despite this limited evidence, guidelines uniformly recommend an antiseptic handwashing agent be used when caring for patients infected or colonized with antimicrobial-resistant organisms (52–54).

5.2 Hand antiseptics

Antimicrobial-resistant organisms do not have a higher frequency of resistance to agents used for hand disinfection when compared to susceptible strains of the same species (55, 56). However, bacteria with intrinsic resistance to some antimicrobials, such as *Providencia stuartii* or *Pseudomonas aeruginosa*, may also have intrinsic resistance to some antiseptics. Thus, where hand antiseptics are used for decontamination, a differential effect for some resistant organisms could be observed. Onesko and Wienke (57) reported, in an uncontrolled study, that introduction of an iodine lotion soap to replace natural soap in two high-prevalence MRSA wards, one an intensive care unit, led to an 80% decrease in nosocomial MRSA. The effect was non-specific, however, as there was a general decrease in other organisms, both susceptible and resistant. Webster et al. (58) reported eradication of MRSA from a neonatal intensive care unit when a triclosan disinfectant replaced chlorhexidine gluconate 4% for handwashing. This was accompanied by an increase in *Pseudomonas aeruginosa* infections, an organism with intrinsic resistance to triclosan (59). Pittet et al. (60) have recently reported that use of an alcohol-based 0.5% chlorhexidine gluconate handrub solution was followed by increased compliance with hand hygiene and a significant decrease over the subsequent four years of all nosocomial infections and MRSA transmission rates. Further comparative studies will be necessary to characterize the impact of specific handwashing practices in containing antimicrobial resistance.

6. Isolation and other barrier practices

6.1 Practices

The use of physical barriers and spatial separation in managing patients with an increased likelihood of transmitting infectious agents to other patients or staff members is a key infection control function. These practices have been variously designated isolation, infection control precautions (61), body substance isolation (62), barrier precautions, standard precautions (63), or routine precautions (64). The interventions usually include identification of patients and patient care activities at risk for transmission of organisms, geographical separation with isolation or cohorting, use of gloves, gowns and other protective equipment by staff to prevent contamination, and ensuring compliance with these practices by staff, patients, and visitors. These precautions have been recommended for several decades for limiting transmission of resistant organisms within acute care facilities (61). Their effectiveness is not well measured, however, and remains controversial in the endemic, rather than the outbreak situation. Available studies usually lack concurrent controls and include multiple simultaneous interventions so the specific role of barrier precautions is seldom defined.

6.2 Enterobacteriaceae

Lucet et al. (65) reported a four-year prospective observational study of nosocomial acquisition of extended spectrum β -lactamase (ESBL)-producing Enterobacteriaceae in a Paris hospital following the introduction of patient screening and barrier precautions. In the first year, the incidence of nosocomial acquisition of these organisms did not decrease. After refinement and re-enforcement of the use of barrier precautions, there was a subsequent decrease from 0.56 to 0.06 cases/100 admissions over the subsequent three years. Concurrent decreases in the incidence of MRSA and *Acinetobacter baumannii* nosocomial transmission were also observed. Similarly, Soulier et al. (66) reported a 40% decrease in ESBL-producing Enterobacteriaceae colonization in a gastrointestinal surgical intensive

care unit with intensified handwashing, single-use equipment, and glove use.

Alford and Hall (43) report a 15-year experience with gentamicin-resistant Enterobacteriaceae in a Veterans' hospital in the United States. Consecutive outbreaks and endemic infection with *Serratia marcescens*, *Klebsiella pneumoniae*, and *Enterobacter cloacae* emerged following acquisition of gentamicin resistance by these organisms. *Pseudomonas aeruginosa* resistant to gentamicin also progressively increased in prevalence. All interventions, including recommended barrier precautions, failed to limit the emergence and nosocomial transmission of these organisms.

6.3 MRSA

Thompson et al. (67) reported the introduction of screening and barrier precautions led to a decrease in MRSA prevalence and incidence in a United States hospital in the subsequent 12 months. In a paediatric intensive care unit, Casseron-Zerbib et al. (68) reported a 90% decrease in MRSA carriage following the introduction of an MRSA containment programme which included increased screening of patients and intensified handwashing, isolation, and other "barrier methods". There was a significant decrease in the overall nosocomial infection rate entirely attributable to a decrease in MRSA infection, although there was no decline in the nosocomial infection rate in transplant patients in the unit. In a Swiss hospital with endemic MRSA, introduction of infection control measures including barrier precautions was followed by a 50% decline in bacteraemia and MRSA isolation over a subsequent five-year period (69). Schmitz et al. (70) also reported the new implementation of barrier practices and intensified environmental cleaning in an intensive care unit with a high rate of endemic MRSA was followed by a decline in transmission of this organism. There are also, however, many reports where decreasing the intensity of barrier precautions for patients infected or colonized with MRSA was not followed by increased rates of

nosocomial transmission or infection (22–28). In addition, Goetz and Muder (39) report a continued increase in MRSA in their institution despite, initially, strict isolation and, subsequently, body substance isolation for all patients. They also observed a periodic variation in the number of MRSA patients which, in the short term, could have been interpreted, as effectiveness of the infection control interventions, but was not sustained.

Souweine et al. (71), in a 10-bed intensive care unit in another French facility, examined retrospectively the impact of introduction of infection control measures including education, surveillance cultures, antiseptic handwashing, gown and gloves, and mupirocin use for patients with MRSA on colonization and infection with antimicrobial-resistant organisms. The overall rate of colonization or infection with MRSA, ESBL-producing *Klebsiella pneumoniae* or multi-resistant *Enterobacter aerogenes* decreased from 15% to 6.8%. The decrease for MRSA was significant between the two periods prior to and following the intervention, but was not significant for the other two organisms. However, the length of stay was also one-third lower in the post-intervention period, at least partially due to promotion of prompt discharge, so some of the observed effect may have been explained by the shorter lengths of stay.

6.4 VRE

In another report from an intensive care unit, VRE acquisition was similar whether gowns with gloves or gloves alone were used for direct patient care (72). Whether handwashing without gloves would have been as effective as gloves was not tested. Bonten et al. (73) reported that nosocomial VRE acquisition in another intensive care unit correlated with “colonization pressure”, but not with compliance with infection control precautions of handwashing and gloving. Brooks et al. (74) studied three different intervention approaches to contain VRE on three different wards. These included enhanced environmental decontamination on one unit, intensive continuing re-education on infection control policies and precautions on a second unit, and replacement of disposable oral and rectal thermometers by tympanic thermometers for all temperatures on a third unit. Thermometer replacement was most effective, and the decrease was sustained at 9 months. There was a short-term decrease in VRE transmission with enhanced environmental sanitation, but this was not sustained at

9 months. There was no decrease and, in fact, an increase at 9 months, for the infection control interventions. Montecalvo et al. (75) reported that “enhanced infection control” which included cohorting of patients and staff, gown and glove use for patients of unknown status, and monitoring compliance was followed by a decrease in infection and colonization with VRE on an adult oncology unit. However, antimicrobial use was also more highly controlled and significantly decreased during the period of intensive infection control interventions, so it is unclear to what extent the extraordinary infection control interventions, or antimicrobial use restriction, contributed to the observed decline.

6.5 Summary

The conflicting observations of the impact of barrier practices in these reports may be explained by differences in study design, target organisms, patient populations, the specific interventions initiated, compliance, level of endemicity of the resistant organism in the facility, concurrent alterations in antimicrobial use, or the normal variation in the natural history of a strain in the population observed. The reports which observed a positive impact usually instituted concurrent controls in addition to barrier precautions. Thus, current evidence to document the effectiveness of patient isolation and other barrier precautions in the containment of resistant organisms in the non-outbreak situation is conflicting, constrained by the limitations of reported studies, and not compelling. If these interventions are effective, the impact is most likely to be observed in selected high-risk patient groups, such as those in intensive care units.

6.6 Standard barrier precautions

Within the past decade, a practice for routine patient care which encourages rigorous hand hygiene and consistent use of gloves and other personal protective equipment whenever contamination is anticipated in the care of any patient has been promoted and widely implemented (52, 63, 64). One rationale for the development of this approach was the inability to consistently identify patients colonized with resistant strains. If this standard of practice is rigorously adhered to, more intense barrier precautions for patients identified as colonized or infected with a resistant organism which may be transmitted by contact should not

provide additional benefit. This is perhaps confirmed, for MRSA, by the many reports where deintensification of barrier precautions have not been associated with an increase in the endemic rate of resistant organisms (24–28). Reports which suggest barrier precautions are effective in containing endemic bacterial resistance are, generally, from facilities which did not follow current recommendations for standard practice (65, 67). The role of specific additional barrier practices for patients colonized or infected with resistant organisms in the context of current practice recommendations has not been determined.

6.7 Multiply-resistant *Mycobacterium tuberculosis*

Another isolation practice is the use of respiratory isolation to prevent transmission of organisms by the airborne route. The continued effectiveness of precautions for the prevention of nosocomial transmission of multiply-drug-resistant tuberculosis after initial outbreak control is convincing evidence that these infection control precautions for airborne transmission are effective (76, 77). They are, of course, equally effective in preventing transmission of drug-susceptible tuberculosis. It was the unique circumstance of exposure of highly susceptible HIV patients and resistant tuberculosis strains which made it apparent that previous practice was not adequate for nosocomial tuberculosis control.

7. Environmental cleaning and sterilization

Sterilization and disinfection of patient care equipment will be equally effective for antimicrobial-resistant and susceptible organisms. As noted in the annex, many outbreaks with resistant organisms have been attributed to inadequate cleaning or disinfection of equipment. Once again, however, the isolation of a resistant organism may have facilitated early identification of the problem.

The role of the hospital environment in acquisition of endemic nosocomial infection remains controversial. For selected organisms, such as fungal infection with hospital construction and *Legionella* infection with water systems, a direct association between the environment and infection is accepted (78). Even without compelling evidence that the environment is a major factor in acquisition of other nosocomial infections, it is accepted that a certain standard of cleanliness and safety is required for hospital environmental surfaces, linen handling, water and food supply, and waste disposal (52). These practices should, of course, limit transmission of both antimicrobial-resistant and susceptible organisms.

There is one report of a decrease in endemic nosocomial infections with aminoglycoside-resistant Gram-negative organisms with environmental interventions alone (79). A high concen-

tration of these organisms was present in the standing water for cut plants. Removal of plants and water, together with daily dry mopping, was temporarily followed by decreased isolation of these resistant organisms in nosocomial infection in patients on the ward. As summarized in the annex to this report, identification of an environmental source, and disinfection or sterilization interventions to control that source have repeatedly been effective in control of outbreaks with resistant organisms.

For both MRSA and VRE the physical environment has been proposed to be an important source for acquisition of these resistant organisms by patients. This is based on repeated observations of substantial contamination of rooms, furniture, and equipment of patients colonized or infected with these organisms (80, 81). More intense house cleaning, including stronger disinfectants and increased frequency of cleaning have been suggested to control endemic transmission (81). However, the evidence for a significant unique role for the environment beyond transmission of organisms on the hands of staff, if there is compliance with recommended normal cleaning practice, is not convincing (21, 74, 82).

8. Antimicrobial Interventions

8.1 Promotion of antimicrobial resistance

The use of prophylactic antimicrobials to prevent infection is an important infection control intervention. However, widespread use of any antimicrobial will ultimately result in emergence of organisms resistant to that agent. Infection control activity, then, may promote antimicrobial resistance. There is a trade-off between the potential decreased requirement for antimicrobials because infections have been prevented, and increased resistance because of antibiotic pressure from prophylactic use. Where the balance lies—beneficial or detrimental, will vary over time and with the perspective—that of the individual patient or of the wider community.

8.2 Systemic prophylaxis

One of the most widely supported uses of prophylaxis is in surgery. For selected surgical procedures, preoperative prophylaxis will decrease post-operative infections (83, 84). However, even with appropriate surgical prophylaxis, some infections will occur post-operatively, and these infections are more likely to be caused by organisms resistant to the antimicrobial used for prophylaxis (85–88). The normal host flora is also altered to a higher prevalence of resistant strains following surgical prophylaxis (88, 89).

In another example, infections which follow systemic antimicrobial prophylaxis for bacterial, fungal, or viral infections in patients with prolonged chemotherapy-induced neutropenia are with organisms resistant to the prophylactic agent. The serial emergence of bacteria resistant to antimicrobials used for prophylaxis has been the impetus for a continuing evolution of antibacterial and antifungal prophylaxis in the neutropenic population (90).

A third example is selective gut decontamination for intensive care unit patients, where topical and systemic antimicrobials are given to prevent nosocomial intensive care unit infection (91). While some studies report a benefit in decreasing respira-

tory infections, improved survival has not been convincingly proven, and this strategy remains controversial (92–94). A consistent theme, however, is the emergence of organisms resistant to antimicrobials used for the prophylactic regimen, contributing to a high prevalence of resistant organisms in the intensive care unit (95–98).

8.3 Topical prophylaxis

The use of topical prophylactic antimicrobials in acute care facilities has also promoted widespread antimicrobial resistance. Topical gentamicin used for the prophylaxis of burn wound infection in the 1970s and 1980s was followed by the widespread emergence of aminoglycoside-resistant Gram-negative organisms which caused large and sustained outbreaks in many burn units (44, 45, 99). In another example, the topical use of an antibiotic ointment at the central line insertion site decreases the risk of line infection, but increases the frequency of infection with *Candida* spp, a more resistant pathogen (100).

8.4 Mupirocin for *S. aureus*

An evolving problem, to a large extent directly attributable to infection control intervention, is the emergence of mupirocin resistance in *Staphylococcus aureus* (101). Initial reports of efficacy of topical mupirocin for eradication of nasal carriage of MRSA (102) led to recommendations for and widespread use of topical mupirocin for decolonization of patients and staff in controlling both outbreak and endemic MRSA. In some units, mupirocin was used for all patients irrespective of whether they had documented MRSA colonization (103, 104). This enthusiastic application of widespread decolonization therapy has been followed by development of a high prevalence of mupirocin-resistant MRSA in reports from different parts of the world (105–108). In one Canadian teaching hospital, mupirocin resistance among MRSA increased from 2.7% to 65% over a three-year

period when used as an adjunct to infection control measures for a continuing MRSA outbreak (107). The increasing use of topical nasal mupirocin for prophylaxis of *S. aureus* infection in high-risk populations, particularly dialysis patients (109, 110) and patients undergoing clean surgical operations (111), would also be expected, ultimately, to lead to increasing mupirocin resistance among both methicillin-susceptible and resistant *S. aureus*.

8.5 Antimicrobial-impregnated medical devices

The introduction of antimicrobial-impregnated medical devices to decrease the frequency of device-related nosocomial infection is a related issue. For short-term central vascular catheters clinical trials suggest a benefit in decreasing line infections with antimicrobial-impregnated lines (112). It is argued that devices incorporating antiseptic substances, such as the silver sulfadiazine cuff (100, 113) or the chlorhexidine-silver sulfadiazine coated

catheter (114), are less likely to promote emergence of resistance than antibiotic-impregnated catheters. However, widespread use of these devices in highly-susceptible intensive care unit patients would still provide optimal conditions for the emergence of resistant strains. Coagulase-negative staphylococci are a particular concern as they are important device-associated pathogens and have repeatedly demonstrated a facility to acquire resistance. Antimicrobials incorporated into other devices, such as the indwelling bladder catheter, have been less convincing in decreasing infection, and are not yet widely used in practice (115). However, there is intense continuing investigation and development of a variety of medical devices which incorporate antimicrobial substances for control of nosocomial infections. Further careful evaluation of these devices will be essential to determine the relative benefits of infection reduction compared with the future risks of antimicrobial resistance.

9. Resources for infection control

9.1 Cost-effectiveness

There is limited information addressing the cost-effectiveness of infection control interventions in containing antimicrobial resistance. The few relevant publications are compromised by methodological problems. The topic is reviewed in detail in another report developed for the Global Forum for Health Research, "Cost-effectiveness analysis: Interventions against antimicrobial resistance" (116). This report also describes the complexities of assessing the costs of antimicrobial resistance and containment, particularly with respect to estimating the impact of current practice into the future.

9.2 Prioritization of infection control resources

There is another aspect of the economic impact of antimicrobial resistance with respect to infection control. For all health care facilities, infection control resources are limited relative to the burden of infections and potential infection control activity. Thus, an infection control programme must always prioritize activity, and reallocation of resources for a new or expanding problem will redistribute resources from other potentially effective programme components. The continuing global increase in MRSA and VRE, in particular, and attempts to comply with recommended comprehensive control

strategies in developed countries, have added a substantial burden to infection control programmes (20,32,39). In most facilities, the increased demands of infection control activity to manage antimicrobial-resistant organisms have not been accompanied by additional infection control resources. Other important activities, such as surveillance, have initially temporarily and sometimes indefinitely, been restricted or lapsed (20). Increased attention to patient care practice to prevent transmission of organisms should, in fact, have a positive impact on all nosocomial infections. However, the disarray in infection control activity occasioned by inordinate demands for antimicrobial resistance control may result in a less effective programme in other areas, with a potential increase in nosocomial infections. The intense focus on resistant organisms, much of which addresses colonization rather than infection, may undermine effective infection control. Infection control programmes in some facilities have successfully obtained increased resources to accommodate the increased activity for antimicrobial resistance containment (68, 89), but this has certainly not been the case universally. In effect, a redirection of the agenda and resources of infection control from preventing infections to containing antimicrobial resistance has a potential to increase all nosocomial infections, hence increasing antimicrobial use and, one assumes, antimicrobial resistance.

10. Resource-poor countries

10.1 Infection control

The interactions of infection control and antimicrobial resistance containment in resource-poor countries need special consideration. Some of the resistant organisms of concern and the impact of antimicrobial resistance on nosocomial infections are similar to the experience in developed countries. However, other organisms, modes of acquisition, or approaches to control may be unique. Many acute care facilities in these countries have no effective infection control activity. In other areas, such as South (117) and Central America (118), South-East Asia (119), and Eastern Europe (120), substantial progress in developing infection control programmes has occurred. There are still, however, limitations in resources and expertise for infection control. A particular deficit which compromises infection control function is limited access to adequate clinical laboratory support.

10.2 Outbreaks with resistant organisms

Information relevant to infection control and antimicrobial resistance in developing countries is primarily found in descriptions of outbreaks attributed to resistant organisms (121–139). Some preliminary summary observations of these reports can be made. First, while the organisms currently of concern in developed countries—MRSA, VRE, and multidrug-resistant Gram-negative bacteria—are observed, over half of these reports describe outbreaks caused by *Salmonella* spp, *Shigella* spp, or *Vibrio cholerae*. These organisms are unusual causes of nosocomial infection in acute care facilities in developed countries today. Secondly, with the exception of the reports from a burn unit (125) and an oncology unit (131), these outbreaks all occurred in neonatal or paediatric units. This likely reflects both the patient population and distribution of resources for care of different patient groups. Finally, in contrast to the reports from developed countries summarized in the annex, the outbreaks reported from developing countries are remarkable

for the limited use of molecular typing methods for characterizing outbreak strains. Molecular typing methods were only reported to have been used for the VRE outbreak in an oncology unit in South Africa (131) and a Tunisian outbreak of *Salmonella wien* (127). This reflects the limited access to clinical microbiology support in many areas.

Several reports provide little information describing control measures instituted to limit the outbreak (121, 127, 132, 133, 139). Clinical presentations and microbiological observations are described rather than epidemiological investigation and intervention. In some cases, control measures were not attempted because of lack of resources. Interventions instituted in other outbreaks were limited, and of a lower intensity than those usually applied in facilities in developed countries. In addition, some of the interventions, such as fumigation, would not be considered useful (128, 130). Several outbreaks were not contained, despite control efforts (122, 125, 128, 138). The resistant strain was, however, eradicated from some institutions (126, 131, 137), particularly where an environmental source (130, 134, 136) or staff carrier (123, 124, 129, 135) was identified. The limitations inherent with publication bias, however, must also be acknowledged for these reports.

10.3 Endemic antimicrobial resistance

A high prevalence of endemic antimicrobial-resistant organisms in acute care facilities in developing countries has been repeatedly reported (140–143). In addition, patients transferred from institutions in developing countries have been the source for introduction of a resistant strain into acute care facilities in a developed country, with subsequent outbreaks due to the resistant organism in the receiving facility (144–146). Thus, endemic antimicrobial resistance is common in health care facilities in developing countries. There is little information, however, which describes the origin, patient risks, or impact of antimicrobial resistance. The effec-

tiveness of infection control measures in these settings in limiting the spread of endemic resistant organisms or preventing infections caused by these organisms is not known.

The current situation in developing countries, with a high prevalence of resistant organisms in health care facilities but rudimentary infection control, may be a potential opportunity. The introduction and monitoring of the impact of infection

control interventions in facilities could permit an evaluation of the effect of infection control programmes and specific activities of these programmes. This is not feasible in developed countries where a relatively higher level of infection control practice is already in place, and the impact of infection control specifically with respect to containment of antimicrobial resistance is difficult to evaluate.

11. Research agenda

Greater in-depth knowledge of the role of an infection control programme in containing antimicrobial resistance in health care facilities is needed. This will also require addressing some basic questions about antimicrobial-resistant strains in health care facilities. For instance, what is the natural history of antimicrobial-resistant strains in patients and the health care environment, and how does antimicrobial therapy modify this? What factors determine spontaneous decline or disappearance of a strain? The burden of illness attributable to resistant organisms, rather than simply the number of organisms, must be measured. Additional studies describing morbidity and mortality directly due to antimicrobial resistance are essential for estimation of the benefits of resistance containment. The global and organism-specific costs of resistance also must be measured. Valid models to support predictions of future costs resulting from loss of efficacy of current antimicrobials are necessary.

The unique contributions of specific infection control interventions to contain resistance must be documented, as the health care system will always function within constrained resources. Which infection control interventions do not provide a benefit, and in which settings? What is the impact of different handwashing agents? When are gloves, or gowns, essential? What is the optimal screening strategy to identify colonized patients? How should the balance between resistance promotion in the long term and short-term benefit of decreased in-

fection in the use of prophylactic antimicrobials be determined? What are the relative benefits of infection control activity and a stringent antimicrobial use programme? What infection control measures are appropriate for health care delivered in the community or long-term care facilities?

There are also many organism-specific questions. Is it more effective to focus control efforts on all *S. aureus*, rather than methicillin-resistant *S. aureus*? In which patient populations might efforts to control VRE be of value? What is the basic microbiology of organism transmission? What conditions enhance organism transmission and how does this vary for different organisms? Is the expansion of ESBL-producing Enterobacteriaceae within a hospital population any different than that observed with susceptible Enterobacteriaceae?

Any serious agenda to contain antimicrobial resistance in health care settings must begin to address the large knowledge gap with respect to the role of infection control. Otherwise, infection control programmes will continue to consume resources and require disruption in patient care in the pursuit of antimicrobial-resistance containment, but in the absence of evidence that these activities are essential. This situation is not, ultimately, sustainable. With such large deficits in understanding, it is not realistic to expect to limit the current progression of resistance emergence and transmission in health care facilities.

12. Discussion

Despite the universal acceptance of infection control as a key element for containment of antimicrobial resistance in acute care facilities, the interactions of infection control and antimicrobial resistance in these settings is complex, and not well studied.

Infection control activity is effective in controlling outbreaks of infection caused by antimicrobial-resistant strains. However, an adequate infection control response is not universally nor consistently effective. In many facilities, outbreak strains have become endemic, despite vigorous and appropriate control measures. The variables which determine success or failure of outbreak control have not been systematically analysed, although it appears that when a point source can be identified control is likely to be achieved. The example of tuberculosis is also evidence that when specific administrative and engineering interventions can be instituted control may also be achieved.

Antimicrobial resistance may also be seen as having a positive impact for infection control. As a phenotypic marker it may facilitate identification of an outbreak strain. The introduction and transmission of a new strain of methicillin-susceptible *S. aureus* into a facility is likely to go unnoticed. A methicillin-resistant strain introduced into a facility without endemic MRSA will be identified as unusual as soon as it is isolated from a clinical specimen. Control measures initiated to limit the transmission of the resistant organism will also decrease transmission of other organisms and, possibly, decrease nosocomial infections globally in patients subject to the interventions. Similarly, contaminated equipment in an intensive care unit may not be recognized if there are a small number of infections with an endemic organism. If the organism is resistant, and this is an unusual phenotype for the unit, it will be identified early and investigation to identify environmental contamination undertaken expeditiously, limiting further infections. Antimicrobial resistance also has likely been beneficial by leading to improvements in standards of patient care. Repeated outbreaks of resistant Gram-

negative organisms in the 1970s led to the recognition of the importance of equipment and care of patients with indwelling catheters, to prevent transmission, leading to current recommendations for care with dedicated equipment, and handwashing and glove use. Similarly, the inherent uncertainty of identifying patients with resistant organisms led to current recommendations for a higher standard of handwashing and glove use for all patient care. These practices will decrease all nosocomial infections. Antimicrobial resistance is certainly not desirable, but clearly has been beneficial for infection control practice.

Evaluating the role of barrier infection control practices in containing endemic antimicrobial resistance is problematic. These practices appear to have some efficacy when they are introduced into high-risk units in facilities where barrier practices have not previously been used. Even in facilities with a high standard of infection control practice, however, these interventions are not sufficient to ultimately prevent the emergence and expansion of resistant organisms. Theoretically, to be effective, barrier interventions must completely interrupt all transfer of microorganisms among patients. If this is achievable, it would only be with the institution of extreme and highly costly measures, including dedicated staff to fully isolate one patient from another. This would require substantial investment in personnel, building infrastructure, and equipment. Such commitment does not seem feasible or appropriate given the current limitations in knowledge of the effectiveness of infection control interventions. Where, and with which patient groups, is the appropriate trade-off between intensity of barrier practice and prevention of transmission of resistant organisms so that containment is feasible and effective? To address this question requires further knowledge of the impacts of antimicrobial resistance, including an estimate of the future loss from decreased antimicrobial efficacy occasioned by current failure to control resistance.

The contribution of infection control to antimicrobial pressure in health care facilities, and the

emergence of antimicrobial resistance through the use of prophylactic topical or systemic antimicrobials should be acknowledged. It is usually assumed that appropriate prophylactic antimicrobial use will decrease infections and lower overall antimicrobial use—a benefit for containing antimicrobial resistance. But resistance follows from antimicrobial use—appropriate or inappropriate—and in this respect the goals of infection control and resistance containment may be divergent. Perhaps the way to frame this problem is to acknowledge that some resolution of the competing priorities of direct patient care, resistance containment, and infection control is necessary, that there is always a threshold at which appropriate antimicrobial use becomes inappropriate use, and this may vary over time.

The goal of an infection control programme is to limit nosocomial infections in patients and staff. The required components for an optimal programme have been determined, and the efficacy of these programmes is well documented. For patient safety, appropriate resources must be made available to support infection control programmes. An effective infection control programme should also reduce infections with antimicrobial-resistant organisms within a global reduction of all nosocomial infections. If infection control programmes

are assigned an additional role of limiting the transmission of organisms between patients to decrease colonization as well as infection, then necessary resources to perform this expanded function should be identified and provided. The redirection of resources from effective infection control activity to antimicrobial resistance control is likely counterproductive, as the overall burden of nosocomial infection may increase. The main focus of infection control must remain on infection reduction.

Within a health care facility, the major determinant of antimicrobial resistance is antimicrobial use. Antimicrobial use leads to the initial emergence of resistance, and is the major determinant of persistence of endemic resistance in a facility. In a sense, infection control programmes and activities attempt to limit the damage created by antimicrobial use practices over which they have little control. The pre-eminent importance of antimicrobial use strategies in containing resistance must be acknowledged. Infection control should not be held accountable for containment of antimicrobial resistance in the absence of aggressive antimicrobial restriction and optimal use promotion in a facility. The development, implementation, and monitoring of an antimicrobial use programme, and the importance of this activity, must be reinforced in any discussion of containment of resistance.

13. Conclusions

Despite a consensus that institutional infection control programmes are important for containing antimicrobial resistance, the interactions between infection control activity and antimicrobial resistance are not straightforward. Optimal infection control programmes, whose goal is to minimize nosocomial infections, may decrease the prevalence of resistance and infections caused by resistant organisms, but may also contribute to the emergence of antimicrobial resistance, and may be more effective in outbreak management because resistance facilitates identification of unusual organisms in the hospital.

The overarching benefit of infection control programmes in decreasing nosocomial infections, some of which may be with resistant organisms, is clear. The extent to which an intensification of in-

fection control activity or expansion of responsibility to include containment of colonization with resistant organisms will benefit either the goal of decreasing nosocomial infections or decreasing endemic antimicrobial resistance cannot be estimated with information currently available. Promoting infection control activity to contain antimicrobial resistance in the absence of effective, highly restrictive, antimicrobial use programmes would appear, ultimately, to be futile. Infection control programmes in health care facilities should be supported and reinforced in their prime role—the prevention of infection, regardless of the presence or absence of antimicrobial resistance. This should lead to optimal patient outcomes, and limit the progression of resistance to the extent that infection control activity may have an impact.

14. Bibliography

1. World Health Organization. *Global Strategy for Containment of Antimicrobial Resistance*. World Health Organization 2001, WHO/CDS/CSR/DRS 2001.2.
2. Goldman DA et al. Strategies to prevent and control the emergence and spread of antimicrobial-resistant microorganisms in hospitals. *JAMA* 1996; 275:234–240.
3. Abbas J et al. *Candida krusei* fungemia: An escalating serious infection in immunocompromised patients. *Arch Intern Med* 2000;160:2659–2664.
4. Bonten MJ et al. Characteristics of polyclonal endemicity of *Pseudomonas aeruginosa* colonization in intensive care units: Implications for infection control. *Amer J Respir Crit Care Med* 1999;160:1212–1219.
5. Wiener J et al. Multiple antibiotic-resistant *Klebsiella* and *Escherichia coli* in nursing homes. *JAMA* 1999;281:517–523.
6. Bonilla HF et al. Colonization with vancomycin-resistant *Enterococcus faecium*: Comparison of a long term care unit with an acute care hospital. *Infect Control Hosp Epidemiol* 1997;18:333–339.
7. Finland M. Changing patterns of susceptibility of common bacterial pathogens to antimicrobial agents. *Ann Intern Med* 1972;76:1009–1036.
8. Moreno F et al. Methicillin-resistant *Staphylococcus aureus* as a community organism. *Clin Infect Dis* 1995;21:1308–1312.
9. Riley LW et al. The significance of hospitals as reservoirs for endemic multiresistant *Salmonella typhimurium* causing infection in urban Brazilian children. *J Infect Dis* 1984;150:236–241.
10. Millar MR et al. Outbreak of infection with penicillin-resistant *Streptococcus pneumoniae* in a hospital for the elderly. *J Hosp Infect* 1994;27:99–104.
11. Lamb VA et al. Outbreak of *Salmonella typhimurium* gastroenteritis due to an imported strain resistant to ampicillin, chloramphenicol, and trimethoprim-sulfamethoxazole in a nursery. *J Clin Microbiol* 1984;20:1076–1079.
12. Robins-Browne RM et al. A hospital outbreak of multiresistant *Salmonella typhimurium* belonging to phage type 193. *J Infect Dis* 1983;147:210–216.
13. US Public Health Action Plan to Combat Antimicrobial Resistance (Part 1: Domestic Issues) 2001. <http://www.cdc.gov/drugresistance/actionplan/index.htm>
14. Health Canada. Controlling Antimicrobial Resistance: An Integrated Action Plan for Canadians. *Can Comm Dis Rep (CCDR)* 1997;Suppl 23S7:1–32.
15. *Opinion of the Scientific Steering Committee on Antimicrobial Resistance*. European Commission DGXXIV 1999. www.europa.eu.int/comm/dg24/health/sc/ssc/out50_en.html
16. Scheckler WE et al. Requirements for infrastructure and essential activities of infection control and epidemiology in hospitals: a consensus panel report. Society of Healthcare Epidemiology of America. *Infect Control Hosp Epidemiol* 1998;19:114–124.
17. Haley RW et al. The efficacy of infection surveillance and control programs in preventing nosocomial infections in US hospitals. *Amer J Epidemiol* 1985;121:182–205.
18. Boyce JM et al. Methicillin-resistant *Staphylococcus aureus*: a briefing for acute care hospitals and nursing facilities. *Infect Control Hosp Epidemiol* 1994; 15:105–113.
19. Mulligan ME et al. Methicillin-resistant *Staphylococcus aureus*: a consensus review of the microbiology, pathogenesis, and epidemiology with implications for prevention and management. *Amer J Med* 1993;94:313–328.
20. Humphreys H, Duckworth G. Methicillin-resistant *Staphylococcus aureus*: a reappraisal of control measures in the light of changing circumstances. *Infect Control Hosp Epidemiol* 1997;36:167–170.
21. Working Party Report. Revised guidelines for the control of methicillin-resistant *Staphylococcus aureus* infection in hospitals. *Jour Hosp Infect* 1998;39:253–290.
22. Adeyemi-Doro FAB et al. Living with methicillin-resistant *Staphylococcus aureus*: A 7-year experience with endemic MRSA in a university hospital. *Infect Control Hosp Epidemiol* 1997;18:765–767.
23. Austin DJ, Anderson RM. Transmission dynamics of epidemic methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant Enterococci in England and Wales. *J Infect Dis* 1999;179:883–891.
24. Harstein AJ et al. Control of methicillin-resistant *Staphylococcus aureus* in a hospital and an intensive care unit. *Infect Control Hosp Epidemiol* 1995; 16:405–411.

25. Cohen SH, Morita MM, Bradford M. A seven year experience with methicillin-resistant *Staphylococcus aureus*. *Amer J Med* 1991;31(suppl 3B):233–237.
26. Guigit M et al. Effectiveness of simple measures to control an outbreak of nosocomial methicillin-resistant *Staphylococcus aureus* infections in an intensive care unit. *Infect Control Hosp Epidemiol* 1990;11:23–26.
27. Ribner BS, Landry MN, Gholson GL. Strict versus modified isolation for prevention of nosocomial transmission of methicillin-resistant *Staphylococcus aureus*. *Infect Control* 1986;7:317–320.
28. Fazal Ba et al. Trends in the prevalence of methicillin-resistant *Staphylococcus aureus* with discontinuation of an isolation policy. *Infect Control Hosp Epidemiol* 1996;17:372–374.
29. Meers PD, Leong KY. The impact of methicillin and aminoglycoside-resistant *Staphylococcus* on the pattern of hospital-acquired infection in an acute hospital. *J Hosp Infect* 1990;16:231–239.
30. Centers for Disease Control and Prevention. Recommendations for preventing the spread of vancomycin resistance: recommendations of the Hospital Infection Control Practices Advisory Committee (HICPAC) *MMWR* 1995;44(RR-12):1–12.
31. Fridkin SK, Gaynes RP. Antimicrobial resistance in intensive care units. *Clin Chest Med* 1999; 20:303–316.
32. Morris J et al. Enterococci resistant to multiple antimicrobial agents, including vancomycin: establishment of endemicity in a university medical center. *Ann Intern Med* 1995;123:250–259.
33. Pegues D et al. Emergence and dissemination of a highly vancomycin-resistant vanA strain of *Enterococcus faecium* at a large teaching hospital. *J Clin Microbiol* 1997;35:1565–1570.
34. Goetz AM et al. Infection and colonization with vancomycin-resistant *Enterococcus faecium* in an acute care Veterans' Affairs Medical Center: a 2-year survey. *Amer J Infect Control* 1998; 26:558–562.
35. Lai KK et al. Failure to eradicate vancomycin resistant enterococci in a university hospital and the cost of barrier precautions. *Infect Control Hosp Epidemiol* 1998;19:647–652.
36. Quale J et al. Experience with a hospital-wide outbreak of vancomycin-resistant enterococci. *Am J Infect Control* 1996;24:372–379.
37. Merrer J et al. "Colonization pressure" and risk of acquisition of methicillin-resistant *Staphylococcus aureus* in a medical intensive care unit. *Infect Control Hosp Epidemiol* 2000;21:718–723.
38. Warshawsky B et al. Hospital and community based surveillance of methicillin-resistant *Staphylococcus aureus*: Previous hospitalization is the major risk factor. *Infect Control Hosp Epidemiol* 2000;21:724–727.
39. Goetz AM, Muder RR. The problem of methicillin-resistant *Staphylococcus aureus*: A critical appraisal of the efficacy of infection control procedures with a suggested approach for infection control programs. *Amer J Infect Control* 1992;20:80–84.
40. Bernards AT et al. Methicillin-resistant *Staphylococcus aureus* and *Acinetobacter baumannii*: An unexpected difference in epidemiologic behaviour. *Am J Infect Control* 1998;26:544–551.
41. Kayser FH. Methicillin-resistant staphylococci 1965–75. *Lancet* 1975;2:650–653.
42. Rosdahl VT, Knudsen AM. The decline of methicillin resistance among Danish staphylococcus strains. *Infect Control Hosp Epidemiol* 1991;21:83–88.
43. Alford AH, Hall A. Epidemiology of infections caused by gentamicin-resistant Enterobacteriaceae and *Pseudomonas aeruginosa* over 15 years at the Nashville Veterans Administration Medical Center. *Rev Infect Dis* 1987;9:1079–1086.
44. Bridges K et al. Gentamicin and silver resistant pseudomonas in a burns unit. *Br Med J* 1979;1:446–479.
45. Snelling CF, et al. Resistance of gram-negative bacilli to gentamicin. *J Infect Dis* 1971;124 (Suppl) S264–272.
46. Mayer KH et al. Molecular evolution, species distribution and clinical consequences of an endemic aminoglycoside resistance plasmid. *Antimicrob Agents Chemother* 1986;29:628–633.
47. Agerton T et al I. Transmission of a highly drug resistant strain of *Mycobacterium tuberculosis*. Community outbreak and nosocomial transmission via a contaminated bronchoscope. *JAMA* 1997;278: 1073–1077.
48. Alvarez M et al. Noscomial outbreak caused by *Scedosporium prolificans* (inflatum): four fatal cases in leukemic patients. *J Clin Microbiol* 1995; 33:3290–3295.
49. Echols RM et al. Multidrug resistant *Serratia marcesens* bacteriuria related to urologic instrumentation. *South Med J* 1984;77:173–177.
50. Larson EA. A causal link between handwashing and risk of infection? Examination of the evidence. *Infect Control Hosp Epidemiol* 1988;9:28–36.
51. Newsom SWB. Pioneers in infection control: Ignaz Philipp Semmelweis. *J Hosp Infect* 1993;23:175–187.
52. Pratt RJ et al, the epic guideline development team. Guidelines for preventing hospital-acquired infections. *J Hosp Infect* 2001;47(Suppl):S3–S4.
53. Larson EL. APIC guideline for handwashing and hand antisepsis in health care settings. *Amer J Infect Control* 1995;23:251–269.

54. Health Canada. Handwashing, cleaning, disinfection, and sterilization in health care. *Can Comm Dis Rep* (CCDR) Supplement, Vol 24S4, July 1998.
55. Russell AD. Bacterial resistance to disinfectants: present knowledge and future problems. *J Hosp Infect* 1999;43(Suppl):S57–68.
56. Jones R. Bacterial resistance and topical antimicrobial wash products. *Am J Infect Control* 1999;27:351–363.
57. Onesko KM, Wienke EC. The analysis of the impact of a mild low-iodine lotion soap on the reduction of nosocomial methicillin-resistant *Staphylococcus aureus*: a new opportunity for surveillance objectives. *Infect Control* 1987;8:284–288.
58. Webster J, Faoagali JL, Cartwright D. Elimination of methicillin-resistant *Staphylococcus aureus* from a neonatal intensive care unit after handwashing with triclosan. *J Paediatr Child Health* 1994;30:59–64.
59. Chuanchuen R et al. Cross-resistance between triclosan and antibiotics in *Pseudomonas aeruginosa* is mediated by multidrug efflux pumps: Exposure of a susceptible mutant strain to triclosan selects nfxB mutants overexpressing MexCD-OprJ. *Antimicrob Agents Chemother* 2001;45:428–432.
60. Pittet D et al. Infection Control Programme. Effectiveness of a hospital-wide programme to improve compliance with hand hygiene. *Lancet* 2000;356:1307–1312.
61. *CDC Isolation techniques for use in hospitals* 2nd Ed. Washington D.C. US Government Printing Office. 1975 (DHEW Publication no. (CDC) 76–8314).
62. Lynch P et al. Rethinking the role of isolation practices in the prevention of nosocomial infections. *Ann Intern Med* 1987;107:243–246.
63. Garner JS. The Hospital Infection Control Practices Advisory Committee: Guidelines for isolation precautions in hospitals. *Infect Control Hosp Epidemiol* 1996;17:53–80.
64. Health Canada. Routine practices and additional precautions for preventing transmission of infection in health care. *Can Comm Dis Rep* (CCDR) Supplement, 25S4, July 1999.
65. Lucet J-C et al. Control of a prolonged outbreak of extended-spectrum beta-lactamase producing Enterobacteriaceae in a university hospital. *Clin Infect Dis* 1999;29:1411–1418.
66. Soulier A et al. Decreased transmission of Enterobacteriaceae with extended-spectrum beta-lactamases in an intensive care unit by nursing reorganization. *J Hosp Infect* 1995;31:89–97.
67. Thompson RL, Cabezudo I, Wenzel RP. Epidemiology of nosocomial infections caused by methicillin-resistant *Staphylococcus aureus*. *Ann Intern Med* 1982;97:309–317.
68. Casseron-Zerbib M et al. A control programme for methicillin-resistant *Staphylococcus aureus* containment in a paediatric intensive care unit: evaluation and impact on infections caused by other organisms. *J Hosp Infect* 1998;40:225–235.
69. Harbarth S et al. Effect of delayed infection control measures on a hospital outbreak of methicillin-resistant *Staphylococcus aureus*. *J Hosp Infect* 2000;46:43–49.
70. Schmitz FJ et al. Methicillin-resistant *Staphylococcus aureus* strains in the greater Dusseldorf area. *Eur J Epidemiol* 1997;13:709–717.
71. Souweine B et al. Role of infection control measures in limiting morbidity associated with multi-resistant organisms in critically ill patients. *J Hosp Infect* 2000;45:107–116.
72. Slaughter S et al. A comparison of the effect of universal use of gloves and gowns with that of glove use alone on the acquisition of vancomycin-resistant enterococci in a medical intensive care unit. *Ann Intern Med* 1996;125:448–456.
73. Bonten MJ et al. The role of “colonization pressure” in the spread of vancomycin-resistant enterococci: an important infection control variable. *Arch Intern Med* 1998;158:1127–1132.
74. Brooks S et al. Reduction in vancomycin-resistant enterococcus and *Clostridium difficile* infections following change in tympanic thermometers. *Infect Control Hosp Epidemiol* 1998;19:333–336.
75. Montecalvo MA et al. Infection-control measures reduce transmission of vancomycin-resistant enterococci in an endemic setting. *Ann Intern Med* 1999;131:269–272.
76. Wenger MN et al. Control of nosocomial transmission of multidrug-resistant *Mycobacterium tuberculosis* among healthcare workers and HIV-infected patients. *Lancet* 1995;345:235–240.
77. Maloney SA et al. Efficacy of control measures in preventing nosocomial transmission of multidrug-resistant tuberculosis to patients and health care workers. *Ann Intern Med* 1995;122:90–95.
78. CDC Guideline for prevention of nosocomial pneumonia. *Respir Care* 1994;39:1191–1236.
79. Taolin D, Merz PM. Flower vases in hospitals as reservoirs of pathogens. *Lancet* 1973;2:1279–1281.
80. Barg NL. Environmental contamination with *Staphylococcus aureus* and outbreaks: the cause or the effect? *Infect Control Hosp Epidemiol* 1993;14:1471–1476.
81. Weber DJ, Rutala WA. Role of environmental contamination in the transmission of VRE. *Infect Control Hosp Epidemiol* 1997;18:306–309.
82. Hayden MK. Insights into the epidemiology and control of infection with vancomycin-resistant enterococci. *Clin Infect Dis* 2000;31:1058–1065.

83. Dellinger EP et al. Quality standard for antimicrobial prophylaxis in surgical procedures. *Infect Control Hosp Epidemiol* 1994;15:182–188.
84. Antibiotic prophylaxis in surgery: Summary of a Swedish-Norwegian Consensus conference. *Scand J Infect Dis* 1998;30:547–557.
85. Ross CB et al. Ceftriaxone versus cefazolin in peripheral arterial operations: a randomized, prospective trial. *South Med J* 1997;90:16–22.
86. Andersen BM et al. Multiply beta-lactam resistant *Enterobacter cloacae* infections linked to the environmental flora in a unit for cardiothoracic and vascular surgery. *Scand J Infect Dis* 1989;21:181–191.
87. Ratto GB et al. Long-term antimicrobial prophylaxis in lung cancer surgery: correlation between microbiological findings and empyema development. *Lung Cancer* 1994;11:345–352.
88. Flynn DM et al. Patients' endogenous flora as the source of nosocomial *Enterobacter* in cardiac surgery. *J Infect Dis* 1987;156:363–368.
89. Terpstra S et al. Rapid emergence of resistant coagulase-negative staphylococci on the skin after antibiotic prophylaxis. *J Hosp Infect* 1999;43:195–202.
90. Hughes WT et al. 1997 guidelines for the use of antimicrobial agents in neutropenic patients with unexplained fever. Infectious Diseases Society of America. *Clin Infect Dis* 1997;25: 551–573.
91. First European Consensus Conference in Intensive Care Medicine. Selective decontamination in intensive care unit patients. *Intensive Care Med* 1992; 18:182–188.
92. D'Amico R et al. Effectiveness of antibiotic prophylaxis in critically ill adult patients: a systematic review of randomized trials. *Br Med J* 1998;316: 1275–1285.
93. Webb CH. Selective decontamination of the digestive tract, SDD: a commentary. *J Hosp Infect* 2000; 46: 106–109.
94. Kollef MH, Fraser VJ. Antibiotic resistance in the intensive care unit. *Ann Infect Med* 2001;134:298–314.
95. Daschner F. Emergence of resistance during selective decontamination of the digestive tract. *Eur J Clin Microbiol Infect Dis* 1992;11:1–3.
96. van Saine HKF et al. Emergence of antibiotic resistance during selective digestive decontamination? *J Hosp Infect* 1992;24:158–161.
97. Webb CH. Antibiotic resistance associated with selective decontamination of the digestive tract. *J Hosp Infect* 1992; 22:1–5.
98. Verwaest C et al. Randomized, controlled trial of selective digestive decontamination in 600 mechanically ventilated patients in a multidisciplinary intensive care unit. *Crit Care Med* 1997;25: 63–71.
99. Shulman JA, Terry PM, Hough CE. Colonization with gentamicin-resistant *Pseudomonas aeruginosa*, pyocine type 5, in a burn unit. *J Infect Dis* 1971;124(Suppl) S18–22.
100. Flowers RH et al. Efficacy of an attachable subcutaneous cuff for the prevention of intravascular catheter-related infection: a randomized controlled trial. *JAMA* 1989;261:878–883.
101. Cookson BD. The emergence of mupirocin resistance: a challenge to infection control and antibiotic prescribing practice. *J Antimicrob Chemother* 1998;41:11–18.
102. Hill RLR, Duckworth GJ, Casewell MW. Elimination of nasal carriage of methicillin-resistant *Staphylococcus aureus* with mupirocin during a hospital outbreak. *J Antimicrob Chemother* 1988; 22:377–384.
103. Mayhall B et al. Blanket use of intranasal mupirocin for outbreak control and long-term prophylaxis of endemic methicillin-resistant *Staphylococcus aureus* in an open ward. *J Hosp Infect* 1996;32: 257–266.
104. Hitomi S et al. Control of a methicillin-resistant *Staphylococcus aureus* outbreak in a neonatal intensive care unit by unselected use of nasal mupirocin ointment. *J Hosp Infect* 2000;46:123–129.
105. Irish D et al. Control of an epidemic methicillin-resistant *Staphylococcus aureus* also resistant to mupirocin. *J Hosp Infect* 1998;39:19–26.
106. Kauffman CA et al. Attempts to eradicate methicillin-resistant *Staphylococcus aureus* from a long-term-care facility with the use of mupirocin ointment. *Am J Med* 1993;94:371–378.
107. Miller MA et al. Development of mupirocin-resistance among methicillin-resistant *Staphylococcus aureus* after widespread use of nasal mupirocin ointment. *Infect Control Hosp Epidemiol* 1996; 17:811–813.
108. Udo EE, Pearman J, Grubb WB. Emergence of high-level mupirocin resistance among methicillin-resistant *Staphylococcus aureus* in Western Australia. *J Hosp Infect* 1994;26:157–165.
109. Boelaert JR et al. The influence of calcium mupirocin nasal ointment on the incidence of *Staphylococcus aureus* infections in haemodialysis patients. *Nephrol Dial Transplant* 1989;4: 278–281.
110. Mupirocin Study Group. Nasal mupirocin prevents *Staphylococcus aureus* exit site infection during peritoneal dialysis. *J Am Soc Nephrol* 1996;7:2403–2408.
111. Mehtar S. New strategies for the use of mupirocin for the prevention of serious infection. *J Hosp Infect* 1998;40 Suppl B:S39–44.
112. Mermel LA. Prevention of intravascular catheter-related infections. *Ann Intern Med* 2000;132:391–402.

113. Maki DG et al. An attachable silver-impregnated cuff for prevention of infection with central vascular catheters: a prospective randomized multicentre trial. *Am J Med* 1988;85:307–314.
114. Maki DG et al. Prevention of central venous catheter-related bloodstream infection by use of an antiseptic-impregnated catheter. A randomized, controlled trial. *Ann Intern Med* 1997;127:257–266.
115. Saint S et al. The efficacy of silver alloy coated urinary catheters in preventing urinary tract infection: a meta-analysis. *Am J Med* 1998;105:236–241.
116. Smith RD et al. *Cost effectiveness analysis: interventions against antimicrobial resistance*. Interim report to the Global Forum for Health Research, 2001 (in preparation).
117. Starling CEF, Couto BRGM, Pinheiro SMC. Applying the Centers for Disease Control and Prevention and National Nosocomial Surveillance System methods in Brazilian hospitals. *Amer J Infect Control* 1997;25:303–311.
118. Ostrosky-Zeichner L et al. Epidemiology of nosocomial outbreaks: 14-year experience in a tertiary care center. *Infect Control Hosp Epidemiol* 2000;21:527–529.
119. Danchavijitr S et al. Efficacy of hospital infection control in Thailand 1988–1992. *J Hosp Infect* 1996;32:147–153.
120. Valinteliene R, Jurkuvenas V, Jepsen OB. Prevalence of hospital-acquired infection in a Lithuanian hospital. *J Hosp Infect* 1996;34:321–329.
121. Akindede JA, Gbadegesin RA. Outbreak of neonatal *Klebsiella* septicaemia at the University College Hospital, Ibadan, Nigeria. Appraisal of predisposing factors and preventive measures. *Trop Geogr Med* 1994;46:151–153.
122. Banerjee M et al. Outbreak of neonatal septicemia with multidrug resistant *Klebsiella pneumoniae*. *Indian J Pediatr* 1993;60:25–27.
123. Buch NA, Dhananjaya A. A nursery outbreak of multidrug resistant *Salmonella typhimurium*. *Indian Pediatr* 1998;35:455–459.
124. Cliff JL, Zinkin P, Martelli A. A hospital outbreak of cholera in Maputo, Mozambique. *Trans R Soc Trop Med Hyg* 1986;80:473–476.
125. Danchavijitr S et al. An outbreak of a methicillin-resistant *Staphylococcus aureus* in a burn unit. *J Med Assoc Thai* 1995 78;(Suppl 1)S11–S14.
126. Haddad Q et al. Outbreak of methicillin-resistant *Staphylococcus aureus* in a neonatal intensive care unit. *J Hosp Infect* 1993;23:211–212.
127. Hammami A et al. Nosocomial outbreak of acute gastroenteritis in a neonatal intensive care unit in Tunisia caused by multiply drug resistant *Salmonella wien* producing SHV-2 beta-lactamase. *Eur J Clin Microbiol Infect Dis* 1991;10:641–646.
128. Joseph AT et al. *Salmonella senftenberg* outbreak in a neonatal unit. *Indian Pediatr* 1990;27:157–160.
129. Kumar A et al. An outbreak of multidrug resistant *Salmonella typhimurium* in a nursery. *Indian Pediatr* 1995;32:881–885.
130. Mahajan R et al. Nosocomial outbreak of *Salmonella typhimurium* in a nursery intensive care unit and paediatric ward. *J Commun Dis* 1995;27:10–14.
131. McCarthy KM et al. Control of an outbreak of vancomycin-resistant *Enterococcus faecium* in an oncology ward in South Africa: effective use of limited resources. *J Hosp Infect* 2000;44:294–300.
132. Mirza NB, Wamola IA. *Salmonella typhimurium* outbreak at Kenyatta National Hospital (1985). *East Afr Med J* 1989;66:453–457.
133. Moss W. An outbreak of gentamicin-resistant *Klebsiella* bacteraemia at a children's hospital. *Ethiopian Med J* 1992;30:197–205.
134. Murphy SA et al. An outbreak of intravenous cannulae associated nosocomial septicaemia due to multidrug-resistant *Klebsiella pneumoniae*. *East Afr Med J* 1994;71:271–272.
135. Nair D et al. *Salmonella senftenberg*: a new pathogen in the burns ward. *Burns* 1999;25:723–727.
136. Newman MJ. Multiple-resistant *Salmonella* group G outbreak in a neonatal intensive care unit. *West Afr Med J* 1996;15:165–169.
137. Orrett FA. Fatal multi-resistant *Pseudomonas aeruginosa* septicemia outbreak in a neonatal intensive care unit in Trinidad. *Ethiopian Med J* 2000;38:85–91.
138. Zaida M et al. Epidemic of *Serratia marcescens* bacteremia and meningitis in a neonatal unit in Mexico City. *Infect Control Hosp Epidemiol* 1989;10:14–20.
139. Chakravarti A, Mandal A, Sharma KB. An outbreak due to multiple drug resistant *Serratia marcescens* in a children's hospital. *Indian J Med Res* 1981;74:196–201.
140. Hart CA, Kariuki S. Antimicrobial resistance in developing countries. *BMJ* 1998;317:647–650.
141. Mehta A et al. A pilot programme of MRSA surveillance in India. *J Postgrad Med* 1996;42:1–3.
142. Vahaboglu H et al. Widespread detection of PER-1-type extended-spectrum beta-lactamases among nosocomial *Acinetobacter* and *Pseudomonas aeruginosa* isolates in Turkey: a nationwide multicenter study. *Antimicrob Agents Chemother* 1997;41:2265–2269.

143. Thevanesam V, Wijeyawardana WL, Ekanayake EW. Methicillin-resistant *Staphylococcus aureus*: The scale of the problem in a Sri Lankan hospital. *J Hosp Infect* 1994;26:123–127.
144. Ransjo U et al. Methicillin-resistant *Staphylococcus aureus* in two burn units: Clinical significance and epidemiologic control. *J Hosp Infect* 1989; 13:355–365.
145. Humphreys H et al. Importation of methicillin-resistant *Staphylococcus aureus* from Baghdad to Dublin and subsequent nosocomial spread. *J Hosp Infect* 1990;15:127–135.
146. Roman RS et al. Rapid geographic spread of a methicillin-resistant *Staphylococcus aureus* strain. *Clin Infect Dis* 1997;25:698–705.

ANNEX

Control of outbreaks of nosocomial antimicrobial-resistant organisms

Legend

1. Outcome: Eradicated if there was a complete disappearance of the outbreak strain; Controlled if the number of cases decreased but did not completely disappear; Failed if there was little or no impact of control measures. When initial interventions were not effective, recorded as “failed”; then subsequent outcome.
2. Reviewed in abstract only; data may be incomplete.
3. UC: unit closed; ED: early diagnosis and presumptive isolation.
4. Penicillin/erythromycin-resistant *S. aureus*; methicillin-susceptible.
5. Vancomycin-intermediate *S. aureus*.
6. Vancomycin-dependent Enterococcus.
7. SDD: selective digestive decontamination.

Reference	Infected/colonized	Intensified Infection Control Practice						Microbiology Support				Antimicrobials				Environmental Reservoir/Carrier	Outcome ¹	
		Hand hygiene	Barriers	Cohort	Education	Environment	Other ²	Screening				Colonized patients	Colonized staff	Restriction	Guidelines			
								Patient	Staff	Environment	Epidemiological typing							
Methicillin-resistant <i>S. aureus</i>																		
Alonso 1997 (1)	10/5		+			+		+	+		+	+						Eradicated
Alvarez 1985 (2)	11	+	+	+	+			+	+		+							Controlled
Andersen 1999 (3)	5/5	+	+			+		+	+		+							Eradicated initially; reintroduced
Arnou 1985 (4)	35	+	+	+		+		+	+	+		+						Controlled
Back 1996 (5)	9/35	+	+	+				+	+		+	+	+					Failed; intense surveillance control
Bacon ² 1987 (6)	30	+	+						+				+					Failed
Barrett 1990 (7)	15	?	+			+	UC	+	+			+						Failed initially; Eradicated/mupirocin
Bartzokas 1984 (8)	6/14	+	+			+		+	+	+		+	+					Controlled
Belani ⁴ 1986 (9)	31	+		+				+	+				+			Nurse carrier		Eradicated
Bitar 1987 (10)	9/9		+	+	+	+		+	+	+			+					Eradicated
Boyce ² 1981 (11)	61							+	+									Failed
Boyce 1983 (12)	151/94	+	+		+	+	UC		+	+			+					Failed
Bradley 1985 (13)	152	+	+					+	+		+	+						Controlled
Campbell 1998 (14)	5/10	+	+	+	+	+		+		+	+							Eradicated
Cetinkaya ² 2000 (15)									+	+	+		+			Surgical dressing container		Not stated
Coovadia 1989 (16)	4/1	+	+	+				+	+	+	+		+			Staff carrier		Eradication
Cotterill 1996 (17)	4/2							+	+							Airborne/exhaust		Eradicated
Cox 1995 (18)	83/317			+		+		+	+		+	+	+					Controlled
Craven 1981 (19)	82/92	+	+					+	+	+	+		+					Controlled
Curry 1993 (20)	?	+	+	+	+							+						Controlled
Dacre 1986 (21)	33/1		+			+		+	+		+	+	+	+				Controlled
Davies 1987 (22)	126	+		+		+	UC		+			+	+					Failed; eradicated with mupirocin
Duckworth 1988 (23)	>500	+		+				+	+		+	+	+					Failed
Dunkle 1981 (24)	32	+	+	+				+	+			+		+				Eradicated
Fang 1993 (25)	28		+						+	+		+	+					Controlled
Farrell ² 1998 (26)	9	+						+	+	+								Eradicated with patient discharge
Farrington 1990 (27)	373	+	+	+	+	+		+	+	+	+							Failure
Goetz 1992 (28)	37/74		+					+	+		+	+	+					Controlled
Guiguet 1990 (29)	14	+	+								+							Controlled

Reference	Infected/colonized	Intensified Infection Control Practice						Microbiology Support				Antimicrobials				Environmental Reservoir/Carrier	Outcome ¹
		Hand hygiene	Barriers	Cohort	Education	Environment	Other ²	Screening				Colonized patients	Colonized staff	Restriction	Guidelines		
								Patient	Staff	Environment	Epidemiological typing						
Methicillin-resistant <i>S. aureus</i> (cont'd)																	
Haddad 1993 (30)	16	+	+	+	+	+	UC		+	+		+	+				Failed; eradicated with mupirocin
Haiduven-Griffiths 1988 (31)	10	+				+			+				+				Controlled
Hartstein 1995 (32)	8	+	+		+				+	+							Controlled
Hill 1988 (33)	>200	+	+	+					+	+		+	+				Failed; controlled with mupirocin
Hill 1984 (34)	33/2	+				+	UC		+	+	+		+	+			Failed; spontaneous resolution
Hitomi 2000 (35)	34	+	+			+			+	+			+	+			Failed; controlled with mupirocin
Irish 1998 (36)	12			+					+	+	+	+	+	+		+	Failed; eradicated with antibiotics
Jernigan 1996 (37)	3/13	+	+		+				+	+		+	+	+			Eradicated
Jones 1999 (38)	26/52	+	+		+	+			+	+			+	+			Eradicated
Klimek 1976 (39)	10/13	+	+						+	+	+	+		+			Eradicated
Kluytmans 1995 (40)	27		+	+		+	HEPA		+	+	+	+	+	+		Food; food handler	Eradicated
Kumari 1998 (41)	6			+		+	UC		+	+	+	+				Ventilation grills	Eradicated
Law 1988 (42)	37/40		+	+		+			+	+		+	+	+			Controlled
Layton 1993 (43)	13	+	+		+	+			+	+	+	+				Blood pressure cuff; shower	Eradicated
Lejeune 1986 (44)	7/10	+	+			+	UC		+	+	+						Eradicated
Lingnau 1994 (45)	?		+		+				+								Controlled
Linnemann 1982 (46)	3/7		+	+	+				+				+				Controlled
Locksley 1982 (47)	28/7		+						+	+		+	+	+			Eradicated
Mayall 1996 (48)	64	+		+	+				+	+			+	+			Failed; controlled with mupirocin
Meier 1996 (49)	4/6	+	+	+	+					+	+	+		+			Failed; eradicated with mupirocin for staff
Millar 1987 (50)	6/2	+		+					+	+		+					Eradicated
Miller 1996 (51)	?		+	+					+				+				Controlled
Moore 1991 (52)	12/43	+	+	+		+	UC		+	+	+		+	+			Eradicated
Murray-Leisure 1990 (53)	173	+	+	+	+				+				+				Failed; controlled with cohorting
Nicolle 1999 (54)	58		+		+				+	+		+	+	+			Eradicated
Parks 1987 (55)	11/16		+						+	+	+	+	+	+		Breast milk	Eradicated
Peacock 1980 (56)	16/15	+	+							+	+	+					Failure

Reference	Infected/colonized	Intensified Infection Control Practice					Microbiology Support				Antimicrobials				Environmental Reservoir/Carrier	Outcome ¹	
		Hand hygiene	Barriers	Cohort	Education	Environment	Other ²	Screening				Colonized patients	Colonized staff	Restriction			Guidelines
								Patient	Staff	Environment	Epidemiological typing						
Methicillin-resistant <i>S. aureus</i> (cont'd)																	
Pearman 1985 (57)	19	+	+	+				+	+		+	+	+				Eradicated
Pina ⁵ 2000 (58)	4/11	+	+					+			+	+					Eradicated
Price 1980 (59)	9/2	+	+	+			UC	+	+	+		+	+				Eradicated
Rao 1988 (60)	12/19		+						+	+		+	+				Controlled
Reboli 1989 (61)	11/15	+	+	+				+	+	+	+						Failed; eradicated with handwashing agent
Rhinehart 1987 (62)	45	+	+		+			+	+		+		+				Failed
Ribner 1989 (63)	3/7	+	+				New Unit	+	+								Controlled
Richardson 1990 (64)	9/3	+	+						+	+	+		+				Eradicated
Roberts ² 1998 (65)	109																Failed
Romance 1991 (66)	4	+	+	+	+			+			+						Eradicated
Ruchel 1999 (67)	89	+		+					+	+	+					Mobile x-ray	Controlled
Schumacher ² – Perdreau 1994 (68)	>30	+	+					+									Controlled
Shanson 1976 (69)	16	+	+			+	UC	+	+	+	+		+				Eradicated
Shanson 1980 (70)	4								+		+		+			Surgeon carrier	Controlled
Shanson 1985 (71)	15	+	+	+			UC	+	+		+		+				Eradicated
Sheretz 1996 (72)	6/2	?	?	?		?			+	+	+		+			Staff carrier	Eradicated
Smith 1998 (73)	6/1	+	+					+			+						Eradicated
Snyder 1993 (74)	9	+	+		+	+					+	+					Eradicated
Storch 1987 (75)	25	+	+	+	+	+		+	+		+		+				Controlled
Tambic 1997 (76)	7/16	+	+					+	+		+	+	+				Eradicated
Tuffnell 1987 (77)	62/68	+		+				+	+		+	+	+				Eradicated
Valls 1994 (78)	117	+	+	+				+	+		+	+	+				Controlled
Vandenbroucke Grauls 1991 (79)	62		+	+		+	UC	+	+	+		+	+				Controlled
Venezia 1992 (80)	7/1					+			+		+		+			Bath tub	Eradicated
Wang ² 2001 (81)	5								+		+		+			Surgeon carrier	Controlled
Ward ² 1981 (82)	66								+			+	+				Controlled
Zafar 1995 (83)	22	+	+	+	+	+		+	+	+		+	+				Failed; controlled with new handwashing agent
Reboli 1990 (61A)	155	+	+	+				+	+		+	+	+				Controlled

Reference	Infected/colonized	Intensified Infection Control Practice						Microbiology Support				Antimicrobials				Environmental Reservoir/Carrier	Outcome ¹
		Hand hygiene	Barriers	Cohort	Education	Environment	Other ²	Screening				Colonized patients	Colonized staff	Restriction	Guidelines		
								Patient	Staff	Environment	Epidemiological typing						
Vancomycin – resistant enterococci																	
Boyce 1994 (84)	37	+	+					+	+	+							Eradicated
Boyce 1995 (85)	4/5		+					+	+	+							Eradicated
Brown 1998 (86)	29	+	+	+		+		+		+				+			Controlled
Chadwick 1996 (87)	35	+			+	+				+	+			+			Controlled; reintroduced
Dominguez 1997 (88)	8		+							+	+						Controlled
Elsner 2000 (89)	5/33	+	+			+				+	+						Controlled
Falk 2000 (90)	4/17	+	+		+	+		+	+	+	+				EKG lead		Eradicated
Handwerger 1993 (91)	9/8	+	+	+		+	UC	+	+	+	+	+	+				Controlled
Hwang ² 1998 (92)	10									+	+				Blood pressure cuff		Controlled
Karanfil 1992 (93)	6	+	+	+	+	+		+	+								Eradicated
Kirkpatrick ⁶ 1999 (94)	5	+	+		+	+		+	+	+				+			Eradicated
Lee 1999 (95)	4		+			+					+						Eradicated
Livonese 1992 (96)	5/13		+			+		+	+	+	+				Electronic thermometer		Eradicated
McCarthy 2000 (97)	34	+	+	+	+	+		+	+	+				+			Eradicated
Nourse ² 2000 (98)	14	+	+			+		+	+	+							Controlled
Pegues 1997 (99)	85/86		+					+		+				+			Failed
Porwancher 1997 (100)	10					+				+					Electronic car probe		Controlled
Rhinehart 1990 (101)	78		+					+	+	+	+						Controlled
Wells 1995 (102)	32/29	+	+					+	+								Failed

Enterobacteriaceae

Acolet 1994 (103)	5/56	+	+	+	+	+	UC	+	+	+	+				Blood gas analyser		Eradicated
Alford 1987 (104)	>1000	+	+		+	+								+	+		Failure; spontaneous disappearance
Anderson 1983 (105)	34	+	+	+				+	+	+		+		+			Failed; controlled with antibiotic restriction
Arroyo ² 1981 (106)	27														+		Eradicated
Bendall 1979 (107)	123													+			Controlled
Bridges 1979 (108)	129			+			UC				+			+	+		Controlled

Reference	Infected/colonized	Intensified Infection Control Practice						Microbiology Support				Antimicrobials				Environmental Reservoir/Carrier	Outcome ¹	
		Hand hygiene	Barriers	Cohort	Education	Environment	Other ²	Screening				Colonized patients	Colonized staff	Restriction	Guidelines			
								Patient	Staff	Environment	Epidemiological typing							
Campbell 1998 (109)	2/5	+	+		+	+		+		+								Eradicated
Casewell 1977 (110)	17	+	+					+	+	+	+							Eradicated
Chow 1979 (111)	15	+	+		+		UC	+	+	+	+							Eradicated
Christensen 1982 (112)	35	+		+	+	+		+	+	+								Eradicated
Coovadia 1992 (113)	3/6	+	+	+	+	+		+	+	+	+		+					Eradicated
Curie 1978 (114)	241	+	+		+	+		+	+	+	+					Urinals/bedpans		Controlled
Dance 1987 (115)	90	+	+					+		+	+							Controlled
Echols 1984 (116)	38								+	+	+					Cystoscope		Spontaneous resolution
Edwards 1974 (117)	10		+					+	+	+						Urinometer		Eradicated
Fierer 1981 (118)	16		+			+		+	+	+		+				Urinals		Controlled
Finnstrom 1998 (119)	4/11	+	+	+				+	+	+	+			+				Failure; controlled with cohort, restriction
Flidel-Rimon 1996 (120)	8	+	+				UC	+	+	+					+			Failed; controlled with unit closure
Forbes 1977 (121)	24/18	?	?												+			Controlled
Gaillot 1998 (122)	3/5					+		+		+	+					Ultrasound gel		Controlled
Gaynes 1984 (123)	16			+				+	+	+	+							Eradicated
Geiseler 1982 (124)	12	?	+						+	+						Urine cylinder		Eradicated
Gerding 1979 (125)	60/6	?	+					+	+	+	+							Controlled
Gruneberg 1979 (126)	38/67							+							+			Controlled
Herra 1998 (127)	7/8	+	?		+				+	+	+							Controlled
Hobson 1996 (128)	283	+	+	+	+	+		+	+	+	+				+			Failed
Hughes 1981 (129)	69	+		+		+		+	+	+	+							Controlled
Kaslow 1976 (130)	127				+		Catheter care				+				+			Controlled
Knowles ² 2000 (131)	24	+	+								+					+		Controlled
Kocka 1980 (132)	35	+	+				Catheter care				+							Controlled
Krieger 1980 (133)	134	+	+	+		+				+						Endoscopy equipment		Controlled

Reference	Infected/colonized	Intensified Infection Control Practice					Microbiology Support				Antimicrobials				Environmental Reservoir/Carrier	Outcome ¹	
		Hand hygiene	Barriers	Cohort	Education	Environment	Other ²	Screening				Colonized patients	Colonized staff	Restriction			Guidelines
								Patient	Staff	Environment	Epidemiological typing						
Lacey 1995 (134)	5		+			+		+	+						Blood gas machine	Eradicated	
Lewis 1983 (135)	5/8	+		+			UC	+	+	+	+				+	Eradication	
Lindsey 1976 (136)	5/6	+	+				Catheter care	+	+	+						Controlled	
Loiwal ² 1999 (137)	13	+		+		+	UC				+				Suction machine	Controlled	
Lucet 1999 (138)	328	+	+	+	+			+								Controlled	
Luzzaro 1998 (139)	30/12		+			+					+					Controlled	
Mayhall ² 1980 (140)	?	+	+					+	+	+						Controlled	
McKee 1982 (141)	26	+	+	+			UC	+	+	+	+					Controlled	
Meyer 1993 (142)	52/103		+											+		Controlled	
Modi 1987 (143)	6/6			+			UC							+		Eradicated	
Morgan 1984 (144)	12/64	+	+	+				+	+	+	+			+	?blood gas machine	Eradicated	
Murphy 1994 (145)	4	+				+										Eradicated	
Mutton 1981 (146)	11	+	+			+	UC		+	+						Failed; eradicated with unit closure	
Patterson 2000 (147)	232	+	+		+			+			+			+		Controlled	
Piagnerelli 2000 (148)	7/5	+	+				UC	+		+	+					Failed; eradicated with unit closure	
Ransjo 1992 (149)	7/1					+		+	+	+	+				Transducer domes	Eradicated	
Rice 1990 (150)	29	+	+							+				+		Controlled	
Rogues 2000 (151)	?	+	+		+	+				+				+	Axillary thermometer	Controlled	
Rutala 1981 (152)	32	+	+						+	+					Urinometers	Eradicated	
Saravolatz 1984 (153)	10	+		+				+	+	+	+			+	+	Eradicated	
Schaberg 1976 (154)	210	+	+		+		Catheter care	+	+	+	+	+		+		Controlled	
Scheidt 1982 (155)	8/22	+	+	+		+				+						Failed; eradicated with cohorting	
Shannon 1998 (156)	3/5	+	+		+			+			+					Eradicated	
Stamm 1976 (157)	8/34	?	+						+	+	+					Controlled	
Taylor 1991 (158)	4/4	+			+	+	UC	+	+	+	+			+	+	Failed; eradicated with SDD ⁷	

Reference	Infected/colonized	Intensified Infection Control Practice					Microbiology Support				Antimicrobials				Environmental Reservoir/Carrier	Outcome ¹	
		Hand hygiene	Barriers	Cohort	Education	Environment	Other ²	Screening				Colonized patients	Colonized staff	Restriction			Guidelines
								Patient	Staff	Environment	Epidemiological typing						

Enterobacteriaceae (cont'd)

van den Berg 2000 (159)	32	+		+		+	UC				+					+	Electronic thermometer	Eradicated	
van der Zwet 1999 (160)	3/10	+		+	+				+		+	+					+		Failed; eradicated with antibiotic change
Wang 1991 (161)	8	+									+	+						Distilled water	Eradicated
Zaidi 1989 (162)	26/6	+					+	UC	+	+	+	+							Eradicated

Pseudomonas aeruginosa

Bert 1998 (163)	27/9	?	+				+	UC				+	+					Enteral solution	Failed; eradicated with ward closure	
Buttery 1998 (164)	8						+					+	+					Toys	Eradicated	
Earnshaw 1985 (165)	5						+					+	+					Endoscope	Eradicated	
Falkiner 1977 (166)	6						+				+	+	+					Urine bottles	Controlled	
Falkiner 1982 (167)	5										+	+	+					Urine bottles	Eradicated	
Garland 1996 (168)	24/6	+			+				+		+	+						Blood gas analyser	Eradicated	
Garcia 1989 (169)	6/2	+	+				+				+	+	+	+					Eradicated	
Gillespie ² 2000 (170)	5						+					+	+					+	Eradicated	
Hsueh 1998 (171)	10	+	+						+	+	+	+							Controlled	
Jumaa 1994 (172)	13					+	+		+		+	+						Suction catheter	Eradicated	
Marrie 1978 (173)	66		+						+	+	+	+						Urinometers	Eradicated	
Orrett 2000 (174)	6										+	+	+					Suction tubing	Eradicated	
Perinpanaygam 1983 (175)	?	+	+									+							Failure	
Richard 1994 (176)	16/4	+	+			+	+					+	+					+	Hydrotherapy	Eradicated
Schelenz 2000 (177)	11	+					+					+	+						Bronchoscopes	Eradicated
Smith 1981 (178)	14	+	+																Eradicated	

Acinetobacter spp

Allen 1987 (179)	14/24	+		+	+	+			+	+	+								Eradicated	
Bernards 1998 (180)	3/19	+	+	+		+	UC		+	+	+	+							Eradicated	
Castle 1978 (181)	3/4	+	+	+	+	+			+	+	+								Controlled	
Cefai 1990 (182)	4/2	+	+			+					+	+							Ventilator tubing	Eradicated

Reference	Infected/colonized	Intensified Infection Control Practice						Microbiology Support				Antimicrobials				Environmental Reservoir/Carrier	Outcome ¹
		Hand hygiene	Barriers	Cohort	Education	Environment	Other ²	Screening				Colonized patients	Colonized staff	Restriction	Guidelines		
								Patient	Staff	Environment	Epidemiological typing						
Acinetobacter spp (cont'd)																	
Contant 1990 (183)	48	+	+			+				+						Temperature probes	Eradicated
Corbella 2000 (184)	153	+	+		+	+	UC			+	+				+		Controlled
Cox 1998 (185)	16	+	+		+	+				+					+		Controlled
Crowe 1995 (186)	11/26	+	+	+		+	UC	+		+	+						Eradicated
D'Agata 2000 (187)	43				+	+		+		+	+						Controlled
French 1980 (188)	39/1	+	+		+	+		+	+	+							Failed; eradicated with intense screening
Go 1994 (189)	59	+	+			+		+	+	+	+						Eradicated
Holton 1982 (190)	58	+	+					+	+	+							Controlled
Kapil ² 1998 (191)	9		+			+				+	+					Heparin ampoules	Controlled
Koeleman 1997 (192)	8/5	+	+	+	+	+	UC				+						Failed; eradicated with ward closure
Levin 1996 (193)	71	+	+	+	+	+				+						Ventilator circuits	Controlled
McDonald 1998 (194)	8					+		+	+	+	+					Air conditioner	Controlled
Pillay 1999 (195)	9	+	+	+		+	UC				+					Suction catheters	Eradicated
Riley 1996 (196)	45	+	+	+		+		+	+	+	+				+		Failure
Sakata 1989 (197)	19/35	+	+	+				+	+	+					+		Controlled
Stone 1985 (198)	9/1	+	+	+		+		+	+	+	+					Resuscitation mouthpiece	Eradicated
Struelens 1993 (199)	2/2	+	+			+				+	+						Controlled; reintroduced
Tankovic 1994 (200)	31	+	+			+	UC		+	+	+				+		Eradicated

Enteric pathogens

Adler 1970 (201)	46	+	+	+		+		+	+	+							Eradicated
Alkan 1982 (202)	33		+					+	+							Patient carrier	Eradicated
Barnass 1989 (203)	17		+	+	+	+		+	+	+		+	+				Eradicated
Buch 1998 (204)	23/4		+	+				+	+	+			+			Staff carrier	Eradicated
Hammami 1991 (205)	27	+				+	UC		+	+	+		+				Eradicated
Joseph 1990 (206)	35					+	UC		+								Failure
Kumar 1995 (207)	21/13							+	+	+						Staff carrier	Eradicated

Reference	Infected/colonized	Intensified Infection Control Practice						Microbiology Support				Antimicrobials				Environmental Reservoir/Carrier	Outcome ¹	
		Hand hygiene	Barriers	Cohort	Education	Environment	Other ²	Screening				Colonized patients	Colonized staff	Restriction	Guidelines			
								Patient	Staff	Environment	Epidemiological typing							
Enteric pathogens (cont'd)																		
Lamb 1984 (208)	5	+	+					+	+	+	+							Eradicated
Mahajan 1995 (209)	48		+			+			+	+							Suction machines	Eradicated
McCall ³ 2000 (210)	14																	Eradication
Newman 1996 (211)	6/21		+			+	UC	+	+	+								Eradication
Pillay 1997 (212)	4/6	+	+	+							+					+		Eradicated
Robins-Browne 1983 (213)	488	+						+	+	+	+							Controlled
Mycobacterium tuberculosis																		
Agerton 1997 (214)	4																Bronchoscope	Spontaneous resolution
Bouvet 1993 (215)	5		+			+	Aerosol											Eradicated
Breathnach 1998 (216)	7		+			+	ED				+							Controlled
Hannan ² 2001 (217)			+			+										+		Controlled
Kenyon 1997 (218)	6		+				ED				+							Controlled
Moro 2000 (219)	116		+				Aerosol				+							Controlled
Rivero 2001 (220)	31		+	+							+							Eradicated
Stroud 1995 (221)	38		+		+	+					+						+	Controlled
Wenger 1995 (222)	?		+			+											+	Controlled
Other																		
de Galan 1999 (223)	36		+						+	+	+	+						Eradicated (<i>S. pneumoniae</i>)
Gould 1987 (224)	5/1							+	+		+							Eradicated (<i>S. pneumoniae</i>)
Hazuka 1977 (225)	3/7		+	+		+	UC	+	+	+								Eradicated (<i>Flavobacterium meningosepticum</i>)
Hekker 1991 (226)	13		+	+				+	+		+	+	+					Eradicated (<i>H. influenzae</i>)
Millar 1994 (227)	15	+					Restrict mobility	+	+									Eradicated (<i>S. pneumoniae</i>)
Nuorti 1998 (228)	11/17						Vaccine	+	+		+					+		Controlled (<i>S. pneumoniae</i>)
Oppenheim 1989 (229)	21				+			+	+	+	+	+		+	+			Eradicated (coagulase-negative Staphylococci)
Orth 1996 (230)	12					+	UC	+	+								Topical moisturizer	Eradicated (<i>Paecilomyces lilacinus</i>)

Reference	Infected/colonized	Intensified Infection Control Practice					Microbiology Support				Antimicrobials				Environmental Reservoir/Carrier	Outcome ¹	
		Hand hygiene	Barriers	Cohort	Education	Environment	Other ²	Screening				Colonized patients	Colonized staff	Restriction			Guidelines
								Patient	Staff	Environment	Epidemiological typing						
Other (cont'd)																	
Patterson 1988 (231)	3/1		+				UC	+	+		+	+					Eradicated (<i>H. influenzae</i>)
Purvis 1991 (232)	13														+		Eradicated (scabies)
Quinn 1984 (23)	5/2	+	+					+	+	+	+						Controlled (JK diphtheroid)
Reboli 1996 (234)	16/22	+				+				+	+					Nebulizer solution	Eradicated (<i>B. cepacia</i>)

Outbreak bibliography

Methicillin-resistant *Staphylococcus aureus*

- Alonso R et al. Outbreak among HIV-infected patients of *Staphylococcus aureus* resistant to cotrimoxazole and methicillin. *Infect Control Hosp Epidemiol* 1997;18:617–621.
- Alvarez S et al. An outbreak of methicillin-resistant *Staphylococcus aureus* eradicated from a large teaching hospital. *Am J Infect Control* 1985;13:115–121.
- Andersen BM et al. A Norwegian nosocomial outbreak of methicillin-resistant *Staphylococcus aureus* resistant to fusidic acid and susceptible to other antistaphylococcal agents. *J Hosp Infect* 1999; 41: 123–132.
- Arnow PM et al. Control of methicillin-resistant *Staphylococcus aureus* in a burn unit: role of nurse staffing. *J Trauma* 1982;22:954–959.
- Back NA et al. Control of methicillin-resistant *Staphylococcus aureus* in a neonatal intensive-care unit: use of intensive microbiologic surveillance and mupirocin. *Infect Control Hosp Epidemiol* 1996; 17:227–231.
- Bacon AE et al. Emergence of nosocomial methicillin-resistant *Staphylococcus aureus* and therapy of colonized personnel during a hospital-wide outbreak. *Infect Control* 1987;8:145–150.
- Barrett SP. The value of nasal mupirocin in containing an outbreak of methicillin-resistant *Staphylococcus aureus* in an orthopaedic unit. *J Hosp Infect* 1990;15:137–142.
- Bartzokas CA et al. Control and eradication of methicillin-resistant *Staphylococcus aureus* on a surgical unit. *N Engl J Med* 1984;311:1422–1425.
- Belani A et al. Outbreak of staphylococcal infection in two hospital nurseries traced to a single nasal carrier. *Infect Control* 1986;7:487–490.
- Bitar CM et al. Outbreak due to methicillin- and rifampin-resistant *Staphylococcus aureus*: epidemiology and eradication of the resistant strain from the hospital. *Infect Control* 1987;8:15–23.
- Boyce JM et al. Epidemiologic studies of an outbreak of nosocomial methicillin-resistant *Staphylococcus aureus* infections. *Infect Control* 1981; 2:110–116.
- Boyce JM et al. Burn units as a source of methicillin-resistant *Staphylococcus aureus* infections. *JAMA* 1983;249:2803–2807.
- Bradley JM et al. Methicillin-resistant *Staphylococcus aureus* in a London hospital. *Lancet* 1985; 1:1493–1495.
- Campbell JR et al. Epidemiological analysis defining concurrent outbreaks of *Serratia marcescens* and methicillin-resistant *Staphylococcus aureus* in a neonatal intensive care unit. *Infect Control Hosp Epidemiol* 1998;19:924–928.
- Cetinkaya Y et al. Analysis of a mini-outbreak of methicillin-resistant *Staphylococcus aureus* in a surgical ward by using arbitrarily primed-polymerase chain reaction. *J Chemother* 2000;12:138–144.
- Coovadia YM et al. A laboratory confirmed outbreak of rifampin-methicillin resistant *Staphylococcus aureus* in a newborn nursery. *J Hosp Infect* 1989;14:303–312.
- Cotterill S, Evans R, Fraise AP. An unusual source for an outbreak of methicillin-resistant *Staphylococcus aureus* on an intensive therapy unit. *J Hosp Infect* 1996;32:207–216.
- Cox RA et al. A major outbreak of methicillin-resistant *Staphylococcus aureus* caused by a new phage-type (EMRSA-16). *J Hosp Infect* 1995;29:87–106.
- Craven DE et al. A large outbreak of infections caused by a strain of *Staphylococcus aureus* resistant to oxacillin and aminoglycosides. *Am J Med* 1981; 71:53–58.
- Curry K et al. Managing an outbreak of *Staphylococcus aureus* in a rehabilitation center. *Rehabil Nurs* 1993;18:240–243, 252.
- Dacre J, Emmerson AM, Jenner EA. Gentamicin-methicillin-resistant *Staphylococcus aureus*: epidemiology and containment of an outbreak. *J Hosp Infect* 1986;7:130–136.
- Davies EA et al. An outbreak of infection with a methicillin-resistant *Staphylococcus aureus* in a special care baby unit: value of topical mupirocin and of traditional methods of infection control. *J Hosp Infect* 1987;10:120–128.
- Duckworth GJ, Lothian JL, Williams JD. Methicillin-resistant *Staphylococcus aureus*: report of an outbreak in a London teaching hospital. *J Hosp Infect* 1988;11:1–15.
- Dunkle LM et al. Eradication of epidemic methicillin-gentamicin-resistant *Staphylococcus aureus* in an intensive care nursery. *Am J Med* 1981;70:455–458.
- Fang FC et al. Value of molecular epidemiologic analysis in a nosocomial methicillin-resistant *Staphylococcus aureus* outbreak. *JAMA* 1993;270:1323–1328.
- Farrell AM et al. An outbreak of methicillin-resistant *Staphylococcus aureus* in a dermatology day-care unit. *Clin Exp Dermatol* 1998;23:249–253.
- Farrington M et al. Outbreaks of infection with methicillin-resistant *Staphylococcus aureus* on neonatal and burn units of a new hospital. *Epidemiol Infect* 1990;105:215–228.
- Goetz MB et al. Management and epidemiologic analyses of an outbreak due to methicillin-resistant *Staphylococcus aureus*. *Am J Med* 1992;92:607–614.

29. Guiguet M et al. Effectiveness of simple measures to control an outbreak of nosocomial methicillin-resistant *Staphylococcus aureus* infections in an intensive care unit. *Infect Control Hosp Epidemiol* 1990; 11: 23–26.
30. Haddad Q et al. Outbreak of methicillin-resistant *Staphylococcus aureus* in a neonatal intensive care unit. *J Hosp Infect* 1993;23:211–222.
31. Haiduven-Griffiths D. Outbreak of methicillin-resistant *Staphylococcus aureus* on a surgical service. *Am J Infect Control* 1988;16:123–127.
32. Hartstein AI et al. Control of methicillin-resistant *Staphylococcus aureus* in a hospital and an intensive care unit. *Infect Control Hosp Epidemiol* 1995; 16:405–411.
33. Hill RL, Duckworth GJ, Casewell MW. Elimination of nasal carriage of methicillin-resistant *Staphylococcus aureus* with mupirocin during a hospital outbreak. *J Antimicrob Chemother* 1988;22:377–384.
34. Hill SF, Ferguson D. Multiply-resistant *Staphylococcus aureus* (bacteriophage type 90) in a special care baby unit. *J Hosp Infect* 1984;5:56–62.
35. Hitomi S et al. Control of a methicillin-resistant *Staphylococcus aureus* outbreak in a neonatal intensive care unit by unselective use of nasal mupirocin ointment. *J Hosp Infect* 2000; 46: 123–129.
36. Irish D et al. Control of an outbreak of an epidemic methicillin-resistant *Staphylococcus aureus* also resistant to mupirocin. *J Hosp Infect* 1998;39:19–26.
37. Jernigan JA et al. Effectiveness of contact isolation during a hospital outbreak of methicillin-resistant *Staphylococcus aureus*. *Am J Epidemiol* 1996; 143:496–504.
38. Jones JW et al. An MRSA outbreak in a urology ward and its association with Nd:YAG coagulation laser treatment of the prostate. *J Hosp Infect* 1999; 41:39–44.
39. Klimek JJ et al. Clinical, epidemiologic, and bacteriologic observations of an outbreak of methicillin-resistant *Staphylococcus aureus* at a large community hospital. *Am J Med* 1976;61:340–345.
40. Kluytmans J et al. Food initiated outbreak of methicillin-resistant *Staphylococcus aureus* analyzed by pheno- and genotyping. *J Clin Microbiol* 1995; 33:1121–1128.
41. Kumari DN et al. Ventilation grilles as a potential source of methicillin-resistant *Staphylococcus aureus* causing an outbreak in an orthopaedic ward at a district general hospital. *J Hosp Infect* 1998;39:127–133.
42. Law MR, Gill ON, Turner A. Methicillin-resistant *Staphylococcus aureus*: associated morbidity and effectiveness of control measures. *Epidemiol Infect* 1988;101:301–309.
43. Layton MC et al. An outbreak of mupirocin-resistant *Staphylococcus aureus* on a dermatology ward associated with an environmental reservoir. *Infect Control Hosp Epidemiol* 1993;14:369–375.
44. Lejeune B et al. Outbreak of gentamicin-methicillin-resistant *Staphylococcus aureus* infection in an intensive care unit for children. *J Hosp Infect* 1986; 7:21–25.
45. Lingnau W, Allerberger F. Control of an outbreak of methicillin-resistant *Staphylococcus aureus* by hygienic measures in a general intensive care unit. *Infection* 1994;2:S135–139.
46. Linnemann CC et al. Methicillin-resistant *Staphylococcus aureus*: experience in a general hospital over four years. *Am J Epidemiol* 1982;115:941–950.
47. Locksley RM et al. Multiply antibiotic resistant *Staphylococcus aureus*: introduction, transmission, and evolution of nosocomial infection. *Ann Intern Med* 1982;97:317–324.
48. Mayall B et al. Blanket use of intranasal mupirocin for outbreak control and long-term prophylaxis of endemic methicillin-resistant *Staphylococcus aureus* in an open ward. *J Hosp Infect* 1996;32:257–266.
49. Meier PA et al. A prolonged outbreak of methicillin-resistant *Staphylococcus aureus* in the burn unit of a tertiary medical center. *Infect Control Hosp Epidemiol* 1996;17:798–802.
50. Millar MR et al. “Methicillin-resistant” *Staphylococcus aureus* in a regional neonatology unit. *J Hosp Infect* 1987;10:187–197.
51. Miller MA et al. Development of mupirocin resistance among methicillin-resistant *Staphylococcus aureus* after widespread use of nasal mupirocin ointment. *Infect Control Hosp Epidemiol* 1996;17:811–813.
52. Moore EP, Williams EW. A maternity hospital outbreak of methicillin-resistant *Staphylococcus aureus*. *J Hosp Infect* 1991;19:5–16.
53. Murray-Leisure KA et al. Control of epidemic methicillin-resistant *Staphylococcus aureus*. *Infect Control Hosp Epidemiol* 1990;11:343–350.
54. Nicolle LE et al. Regional dissemination and control of epidemic methicillin-resistant *Staphylococcus aureus*. *Infect Control Hosp Epidemiol* 1999;20:202–205.
55. Parks YA et al. Methicillin resistant *Staphylococcus aureus* in milk. *Arch Dis Child* 1987;62:82–84.
56. Peacock JE, Marsik FJ, Wenzel RP. Methicillin-resistant *Staphylococcus aureus*: introduction and spread within a hospital. *Ann Intern Med* 1980; 93:526–532.
57. Pearman JW et al. Control of a methicillin-resistant *Staphylococcus aureus* in an Australian metropolitan teaching hospital complex. *Med J Aust* 1985; 142:103–108.

58. Pina P et al. An outbreak of *Staphylococcus aureus* strains with reduced susceptibility to glycopeptides in a French general hospital. *Clin Infect Dis* 2000; 31:1306–1308.
59. Price EH, Brain A, Dickson JA. An outbreak of infection with a gentamicin and methicillin-resistant *Staphylococcus aureus* in a neonatal unit. *J Hosp Infect* 1980;1:221–228.
60. Rao N, Jacobs S, Joyce L. Cost-effective eradication of an outbreak of methicillin-resistant *Staphylococcus aureus* in a community teaching hospital. *Infect Control Hosp Epidemiol* 1988; 9: 255–260.
61. Reboli AC, John JF, Levkoff AH. Epidemic methicillin-gentamicin-resistant *Staphylococcus aureus* in a neonatal intensive care unit. *Am J Dis Child* 1989; 143: 34–39.
- 61A. Reboli AC et al. Methicillin-resistant *Staphylococcus aureus* outbreak at a Veteran's Affairs Medical Center: Importance of carriage of the organism by hospital personnel. *Infect Control Hosp Epidemiol* 1990;11:291–296.
62. Rhinehart E et al. Nosocomial clonal dissemination of methicillin-resistant *Staphylococcus aureus*. Elucidation by plasmid analysis. *Arch Intern Med* 1987; 147:521–524.
63. Ribner BS et al. Outbreak of multiply resistant *Staphylococcus aureus* in a pediatric intensive care unit after consolidation with a surgical intensive care unit. *Am J Infect Control* 1989;17:244–249.
64. Richardson JF et al. Beta-lactamase-negative, methicillin-resistant *Staphylococcus aureus* in a newborn nursery: report of an outbreak and laboratory investigations. *J Hosp Infect* 1990;109–121.
65. Roberts RB et al. Outbreak in a New York teaching hospital burn center caused by the Iberian epidemic clone of MRSA. *Microb Drug Resist* 1998;4:175–183.
66. Romance L et al. An outbreak of methicillin-resistant *Staphylococcus aureus* in a pediatric hospital—how it got away and how we caught it. *Can J Infect Control* 1991;6:11–13.
67. Ruchel R et al. Outbreak of methicillin-resistant *Staphylococcus aureus* in a German tertiary-care hospital. *Infect Control Hosp Epidemiol* 1999;20:353–355.
68. Schumacher-Perdreau F et al. Outbreak of methicillin-resistant *Staphylococcus aureus* in a teaching hospital—epidemiological and microbiological surveillance. *Zentralbl Bakteriol* 1994;280:550–559.
69. Shanson DC, Kensit JC, Duke R. Outbreak of hospital infection with a strain of *Staphylococcus aureus* resistant to gentamicin and methicillin. *Lancet* 1976;1347–1348.
70. Shanson DC, McSwiggan DA. Operating theatre acquired infection with a gentamicin-resistant strain of *Staphylococcus aureus*: outbreaks in two hospitals attributable to one surgeon. *J Hosp Infect* 1980; 1:171–172.
71. Shanson DC, Johnstone D, Midgley J. Control of a hospital outbreak of methicillin-resistant *Staphylococcus aureus* infections: value of an isolation unit. *J Hosp Infect* 1985; 6:285–292.
72. Sheretz RJ et al. A cloud adult: the *Staphylococcus aureus*-virus interaction revisited. *Ann Intern Med* 1996;124:539–547.
73. Smith NP et al. An outbreak of methicillin-resistant *Staphylococcus aureus* infection in HIV-seropositive persons. *Int J STD AIDS* 1998;9:726–730.
74. Snyder LL et al. Methicillin-resistant *Staphylococcus aureus* in a burn center. *J Burn Care Rehabil* 1993; 14:(2Pt1):164–168.
75. Storch GA et al. Methicillin-resistant *Staphylococcus aureus* in a nursing home. *Infect Control* 1987;8:24–29.
76. Tambic A et al. Analysis of an outbreak of non-phage-typable methicillin-resistant *Staphylococcus aureus* by using a randomly amplified polymorphic DNA assay. *J Clin Microbiol* 1997;35:3092–3097.
77. Tuffnell DJ et al. Methicillin resistant *Staphylococcus aureus*; the role of antiseptics in the control of an outbreak. *J Hosp Infect* 1987;10:255–259.
78. Valls V et al. Long-term efficacy of a program to control methicillin-resistant *Staphylococcus aureus*. *Eur J Clin Microbiol Infect Dis* 1994;13:90–95.
79. Vandenbroucke-Grauls CM et al. Control of epidemic methicillin-resistant *Staphylococcus aureus* in a Dutch university hospital. *Eur J Clin Microbiol Infect Dis* 1991;10:6–11.
80. Venezia RA et al. Investigation of an outbreak of methicillin-resistant *Staphylococcus aureus* in patients with skin disease using DNA restriction patterns. *Infect Control Hosp Epidemiol* 1992;13:472–476.
81. Wang JT et al. A hospital-acquired outbreak of methicillin-resistant *Staphylococcus aureus* infection initiated by a surgeon carrier. *J Hosp Infect* 2001; 47:104–109.
82. Ward TT et al. Observations relating to an inter-hospital outbreak of methicillin-resistant *Staphylococcus aureus*: role of antimicrobial therapy in infection control. *Infect Control* 1981;2:453–459.
83. Zafar AB et al. Use of 0.3% triclosan to eradicate an outbreak of methicillin-resistant *Staphylococcus aureus* in a neonatal nursery. *Am J Infect Control* 1995;23:200–208.

Vancomycin-resistant enterococci

84. Boyce JM et al. Outbreak of multidrug-resistant *Enterococcus faecium* with transferable vanB class vancomycin resistance. *J Clin Microbiol* 1994; 32: 1148–1153.

85. Boyce JM et al. Controlling vancomycin-resistant enterococci. *Infect Control Hosp Epidemiol* 1995; 16:634–637.
 86. Brown AR et al. Epidemiology and control of vancomycin-resistant enterococci in a renal unit. *J Hosp Infect* 1998;40:115–124.
 87. Chadwick PR et al. Epidemiology of an outbreak due to glycopeptide-resistant *Enterococcus faecium* on a leukaemia unit. *J Hosp Infect* 1996;34:171–182.
 88. Dominguez EA et al. An outbreak of vancomycin-resistant *Enterococcus faecium* in liver transplant recipients. *Liver Transpl Surg* 1997;3:586–590.
 89. Elsner HA et al. Nosocomial outbreak of vancomycin-resistant *Enterococcus faecium* at a German university pediatric hospital. *Int J Hyg Environ Health* 2000;203:147–152.
 90. Falk PS et al. Outbreak of vancomycin-resistant enterococci in a burn unit. *Infect Control Hosp Epidemiol* 2000; 21: 575–582.
 91. Handwerger S et al. Nosocomial outbreak due to *Enterococcus faecium* highly resistant to vancomycin, penicillin, and gentamicin. *Clin Infect Dis* 1993; 16:750–755.
 92. Hwang YS et al. Investigation of an outbreak of vancomycin-resistant *Enterococcus faecium* in a low prevalence university hospital. *J Investig Med* 1998;46:435–443.
 93. Karanfil LV et al. A cluster of vancomycin-resistant *Enterococcus faecium* in an intensive care unit. *Infect Control Hosp Epidemiol* 1992;13:195–200.
 94. Kirkpatrick BD et al. An outbreak of vancomycin-dependent *Enterococcus faecium* in a bone marrow transplant unit. *Clin Infect Dis* 1999; 29: 1268–1273.
 95. Lee HK, Lee WG, Cho SR. Clinical and molecular biological analysis of a nosocomial outbreak of vancomycin-resistant enterococci in a neonatal intensive care unit. *Acta Paediatr* 1999;88:651–654.
 96. Livornese LL et al. Hospital-acquired infection with vancomycin-resistant *Enterococcus faecium* transmitted by electronic thermometers. *Ann Intern Med* 1992;117:112–116.
 97. McCarthy KM et al. Control of an outbreak of vancomycin-resistant *Enterococcus faecium* in an oncology ward in South Africa: effective use of limited resources. *J Hosp Infect* 2000;44:294–300.
 98. Nourse C et al. Eradication of vancomycin-resistant *Enterococcus faecium* from a paediatric oncology unit and prevalence of colonization in hospitalized and community-based children. *Epidemiol Infect* 2000; 124:53–59.
 99. Pegues DA et al. Emergence and dissemination of a highly vancomycin-resistant vanA strain of *Enterococcus faecium* at a large teaching hospital. *J Clin Microbiol* 1997;35:1565–1570.
 100. Porwancher R et al. Epidemiological study of hospital-acquired infection with vancomycin-resistant *Enterococcus faecium*: possible transmission by an electronic ear-probe thermometer. *Infect Control Hosp Epidemiol* 1997;18:771–773.
 101. Rhinehart E et al. Rapid dissemination of beta-lactamase producing, aminoglycoside-resistant *Enterococcus faecalis* among patients and staff on an infant-toddler surgical ward. *N Engl J Med* 1990; 323: 1814–1818.
 102. Wells CL et al. Stool carriage, clinical isolation, and mortality during an outbreak of vancomycin-resistant enterococci in hospitalized medical and/or surgical patients. *Clin Infect Dis* 1995; 21: 45–50.
- Enterobacteriaceae (other than enterics)**
103. Acolet D et al. *Enterobacter cloacae* in a neonatal intensive care unit: account of an outbreak and its relationship to use of third generation cephalosporins. *J Hosp Infect* 1994; 28: 273–286.
 104. Alford RH, Hall A. Epidemiology of infections caused by gentamicin-resistant Enterobacteriaceae and *Pseudomonas aeruginosa* over 15 years at the Nashville Veterans' Administration Medical Center. *Rev Infect Dis* 1987;9:1079–1086.
 105. Anderson EL, Hieber JP. An outbreak of gentamicin-resistant *Enterobacter cloacae* infections in a pediatric intensive care unit. *Infect Control* 1983;4:148–152.
 106. Arroyo JC et al. Clinical, epidemiologic and microbiologic features of a persistent outbreak of amikacin-resistant *Serratia marcescens*. *Infect Control* 1981;2:367–372.
 107. Bendall MJ, Gruneberg RN. An outbreak of infection caused by trimethoprim-resistant coliform bacilli in a geriatric unit. *Age Ageing* 1979;8:231–236.
 108. Bridges K et al. Gentamicin and silver-resistant pseudomonas in a burns unit. *Br Med J* 1979; 1:446–449.
 109. Campbell JR et al. Epidemiological analysis defining concurrent outbreaks of *Serratia marcescens* and methicillin-resistant *Staphylococcus aureus* in a neonatal intensive-care unit. *Infect Control Hosp Epidemiol* 1998;19:924–928.
 110. Casewell MW et al. Gentamicin-resistant *Klebsiella aerogenes* in a urological ward. *Lancet* 1977;2:444–446.
 111. Chow AW et al. A nosocomial outbreak of infections due to multiply resistant *Proteus mirabilis*: role of intestinal colonization as a major reservoir. *J Infect Dis* 1979;139:621–627.

112. Christensen GD et al. Epidemic *Serratia marcescens* in a neonatal intensive care unit: importance of the gastrointestinal tract as a reservoir. *Infect Control* 1982;3:127–133.
113. Coovadia YM et al. Multiresistant *Klebsiella pneumoniae* in a neonatal nursery: the importance of maintenance of infection control policies and procedures in the prevention of outbreaks. *J Hosp Infect* 1992;22:197–205.
114. Curie K et al. A hospital epidemic caused by gentamicin-resistant *Klebsiella aerogenes*. *J Hyg (Lond)* 1978;80:115–123.
115. Dance DA et al. A hospital outbreak caused by a chlorhexidine and antibiotic-resistant *Proteus mirabilis*. *J Hosp Infect* 1987;10:10–16.
116. Echols RM et al. Multidrug-resistant *Serratia marcescens* bacteriuria related to urologic instrumentation. *South Med J* 1984;77:173–177.
117. Edwards LD et al. Outbreak of a nosocomial infection with a strain of *Proteus rettgeri* resistant to many antimicrobials. *Am J Clin Pathol* 1974;61:41–46.
118. Fierer J, Ekstrom M. An outbreak of *Providencia stuartii* urinary tract infections. Patients with condom catheters are a reservoir of the bacteria. *JAMA* 1981;245:1553–1555.
119. Finnstrom O et al. Control of an outbreak of a highly beta-lactam-resistant *Enterobacter cloacae* strain in a neonatal special care unit. *Acta Paediatr* 1998;87:1070–1074.
120. Flidel-Rimon O et al. An outbreak of antibiotic multiresistant *Klebsiella* at the neonatal intensive care unit, Kaplan Hospital, Rehovot, Israel, November 1991 to April 1992. *Am J Perinatol* 1996;13:99–102.
121. Forbes I et al. The emergence of gentamicin-resistant klebsiellae in a large general hospital. *Med J Aust* 1977;1:14–16.
122. Gaillot O et al. Nosocomial outbreak of *Klebsiella pneumoniae* producing SHV-5 extended-spectrum beta-lactamase, originating from a contaminated ultrasonography coupling gel. *J Clin Microbiol* 1998;36:1357–1360.
123. Gaynes RP et al. A nursery outbreak of multiple-aminoglycoside-resistant *Escherichia coli*. *Infect Control* 1984;5:519–524.
124. Geiseler PJ, Harris B, Andersen BR. Nosocomial outbreak of nitrate-negative *Serratia marcescens* infections. *J Clin Microbiol* 1982;15:728–730.
125. Gerding DN et al. Nosocomial multiply-resistant *Klebsiella pneumoniae*: epidemiology of an outbreak of apparent index case origin. *Antimicrob Agents Chemother* 1979;15:608–615.
126. Gruneberg RN, Bendall MJ. Hospital outbreak of trimethoprim resistance in pathogenic coliform bacteria. *Br Med J* 1979;2:7–9.
127. Herra CM et al. An outbreak of an unusual strain of *Serratia marcescens* in two Dublin hospitals. *J Hosp Infect* 1998;39:135–141.
128. Hobson RP, MacKenzie FM, Gould IM. An outbreak of multiply-resistant *Klebsiella pneumoniae* in the Grampian region of Scotland. *J Hosp Infect* 1996;33:249–262.
129. Hughes VM, Henderson WG, Datta N. Discrimination between multiply-resistant klebsiella strains during a hospital outbreak: use of klebecin-typing and a screening test for plasmids. *J Hosp Infect* 1981;2:45–54.
130. Kaslow RA et al. Nosocomial infection with highly resistant *Proteus rettgeri*. Report of an outbreak. *Am J Epidemiol* 1976;104:278–286.
131. Knowles S et al. An outbreak of multiply resistant *Serratia marcescens*: the importance of persistent carriage. *Bone Marrow Transplant* 2000;25:873–877.
132. Kocka FE et al. Nosocomial multiply resistant *Providencia stuartii*: a long-term outbreak with multiple biotypes and serotypes at one hospital. *J Clin Microbiol* 1980;11:167–169.
133. Krieger JN et al. A nosocomial epidemic of antibiotic-resistant *Serratia marcescens* urinary tract infections. *J Urol* 1980;124:498–502.
134. Lacey SL, Want SV. An outbreak of *Enterobacter cloacae* associated with contamination of a blood gas machine. *J Infect* 1995;30:223–226.
135. Lewis DA et al. Infection with netilmicin resistant *Serratia marcescens* in a special care baby unit. *Br Med J (Clin Res Ed)* 1983;287:1701–1705.
136. Lindsey JO et al. An outbreak of nosocomial *Proteus rettgeri* urinary tract infection. *Am J Epidemiol* 1976;103:2461–2469.
137. Loiwal V et al. *Enterobacter aerogenes* outbreak in a neonatal intensive care unit. *Pediatr Int* 1999;41:157–161.
138. Lucet JC et al. Control of a prolonged outbreak of extended-spectrum beta-lactamase-producing enterobacteriaceae in a university hospital. *Clin Infect Dis* 1999;29:1411–1418.
139. Luzzaro F et al. Repeated epidemics caused by extended-spectrum beta-lactamase-producing *Serratia marcescens* strains. *Eur J Clin Microbiol Infect Dis* 1998;17:629–636.
140. Mayhall CG et al. Nosocomial klebsiella infection in a neonatal unit: identification of risk factors for gastrointestinal colonization. *Infect Control* 1980;1:239–246.
141. McKee KT et al. Nursery epidemic due to multiply-resistant *Klebsiella pneumoniae*: epidemiologic setting and impact on perinatal health care delivery. *Infect Control* 1982;3:150–156.

142. Meyer KS et al. Nosocomial outbreak of *Klebsiella* infection resistant to late-generation cephalosporins. *Ann Intern Med* 1993;119:353–358.
143. Modi N, Damjanovic V, Cooke RW. Outbreak of cephalosporin resistant *Enterobacter cloacae* infection in a neonatal intensive care unit. *Arch Dis Child* 1987;62:148–151.
144. Morgan ME, Hart CA, Cooke RW. *Klebsiella* infection in a neonatal intensive care unit: role of bacteriological surveillance. *J Hosp Infect* 1984; 5:377–385.
145. Murphy SA et al. An outbreak of intravenous cannula associated nosocomial septicaemia due to multidrug-resistant *Klebsiella pneumoniae*. *East Afr Med J* 1994;71:271–272.
146. Mutton KJ, Brady LM, Harkness JL. *Serratia* cross-infection in an intensive therapy unit. *J Hosp Infect* 1981;2:85–91.
147. Patterson JE et al. Association of antibiotic utilization measures and control of multiple-drug resistance in *Klebsiella pneumoniae*. *Infect Control Hosp Epidemiol* 2000;21:455–458.
148. Piagnerelli M et al. Outbreak of nosocomial multidrug-resistant *Enterobacter aerogenes* in a geriatric unit: failure of isolation contact, analysis of risk factors, and use of pulsed-field gel electrophoresis. *Infect Control Hosp Epidemiol* 2000; 21:651–653.
149. Ransjo U et al. An outbreak of *Klebsiella oxytoca* septicemias associated with the use of invasive blood pressure monitoring equipment. *Acta Anaesthesiol Scand* 1992;36:289–291.
150. Rice LB et al. Outbreak of ceftazidime resistance caused by extended-spectrum beta-lactamases at a Massachusetts chronic-care facility. *Antimicrob Agents Chemother* 1990; 34: 2193–2199.
151. Rogues AM et al. Thermometers as a vehicle for transmission of extended-spectrum-beta-lactamase producing *Klebsiella pneumoniae*. *J Hosp Infect* 2000;45:76–77.
152. Rutala WA et al. *Serratia marcescens* nosocomial infections of the urinary tract associated with urine measuring containers and urinometers. *Am J Med* 1981;70:659–663.
153. Saravolatz LD et al. An outbreak of gentamicin-resistant *Klebsiella pneumoniae*: analysis of control measures. *Infect Control* 1984;5:79–84.
154. Schaberg DR et al. An outbreak of nosocomial infections due to multiply resistant *Serratia marcescens*: evidence of interhospital spread. *J Infect Dis* 1976;134:181–188.
155. Scheidt A et al. Nosocomial outbreak of resistant *Serratia* in a neonatal intensive care unit. *NY State J Med* 1982;82:1188–1191.
156. Shannon K et al. A hospital outbreak of extended-spectrum beta-lactamase-producing *Klebsiella pneumoniae* investigated by RAPD typing and analysis of the genetics and mechanisms of resistance. *J Hosp Infect* 1998;39:291–300.
157. Stamm WE et al. A nursery outbreak caused by *Serratia marcescens*—scalp-vein needles as a portal of entry. *J Pediatr* 1976;89:96–99.
158. Taylor ME, Oppenheim BA. Selective decontamination of the gastrointestinal tract as an infection control measure. *J Hosp Infect* 1991;17:271–278.
159. van den Berg RW et al. *Enterobacter cloacae* outbreak in the NICU related to disinfected thermometers. *J Hosp Infect* 2000;45:29–34.
160. van der Zwet WC et al. Nosocomial outbreak of gentamicin-resistant *Klebsiella pneumoniae* in a neonatal intensive care unit controlled by a change in antibiotic policy. *J Hosp Infect* 1999;42:295–302.
161. Wang CC et al. Analysis of plasmid pattern in paediatric intensive care unit outbreaks of nosocomial infection due to *Enterobacter cloacae*. *J Hosp Infect* 1991;19:33–40.
162. Zaidi M et al. Epidemic of *Serratia marcescens* bacteremia and meningitis in a neonatal unit in Mexico City. *Infect Control Hosp Epidemiol* 1989; 10:14–20.

Pseudomonas aeruginosa

163. Bert F et al. Multi-resistant *Pseudomonas aeruginosa* outbreak associated with contaminated tap water in a neurosurgery intensive care unit. *J Hosp Infect* 1998;39:53–62.
164. Buttery JP et al. Multiresistant *Pseudomonas aeruginosa* in a pediatric oncology ward related to bath toys. *Pediatr Infect Dis J* 1998;17:509–513.
165. Earnshaw JJ, Clark AW, Thom BT. Outbreak of *Pseudomonas aeruginosa* following endoscopic retrograde cholangiopancreatography. *J Hosp Infect* 1985;6:95–97.
166. Falkiner FR et al. Cross infection in a surgical ward caused by *Pseudomonas aeruginosa* with transferable resistance to gentamicin and tobramycin. *J Clin Pathol* 1977;30:731–737.
167. Falkiner FR et al. Amikacin, gentamicin and tobramycin resistant *Pseudomonas aeruginosa* in a leukaemic ward. Epidemiology and genetic studies. *J Hosp Infect* 1982;3:253–261.
168. Garland SM et al. *Pseudomonas aeruginosa* outbreak associated with a contaminated blood-gas analyser in a neonatal intensive care unit. *J Hosp Infect* 1996;33:145–151.
169. Garcia DC et al. An outbreak of multiply resistant *Pseudomonas aeruginosa* in a neonatal unit: plasmid pattern analysis. *J Hosp Infect* 1989;14:99–105.

170. Gillespie TA et al. Eradication of a resistant *Pseudomonas aeruginosa* strain after a cluster of infections in a hematology/oncology unit. *Clin Microbiol Infect* 2000;6:125–130.
171. Hsueh PR et al. Persistence of a multidrug-resistant *Pseudomonas aeruginosa* clone in an intensive care burn unit. *J Clin Microbiol* 1998;36:1347–51.
172. Jumaa P, Chattopadhyay B. Outbreak of gentamicin, ciprofloxacin-resistant *Pseudomonas aeruginosa* in an intensive care unit, traced to contaminated quivers. *J Hosp Infect* 1994;28:209–218.
173. Marrie TJ et al. Prolonged outbreak of nosocomial urinary tract infection with a single strain of *Pseudomonas aeruginosa*. *Can Med Assoc J* 1978;119:593–596.
174. Orrett FA. Fatal multi-resistant *Pseudomonas aeruginosa* septicemia outbreak in a neonatal intensive care unit in Trinidad. *Ethiop Med J* 2000;38:85–91.
175. Perinpanaygam RM, Grundy HC. Outbreak of gentamicin-resistant *Pseudomonas aeruginosa* infection in a burns unit. *J Hosp Infect* 1983;4:71–73.
176. Richard P et al. *Pseudomonas aeruginosa* outbreak in a burn unit: role of antimicrobials in the emergence of multiply resistant strains. *J Infect Dis* 1994;170:377–383.
177. Schelenz S, French G. An outbreak of multidrug-resistant *Pseudomonas aeruginosa* infection associated with contamination of bronchoscopes and an endoscope washer-disinfector. *J Hosp Infect* 2000;46:23–30.
178. Smith PW, Rusnak PG. Aminoglycoside-resistant *Pseudomonas aeruginosa* urinary tract infection: study of an outbreak. *J Hosp Infect* 1981;2:71–75.
183. Contant J et al. Investigation of an outbreak of *Acinetobacter calcoaceticus* var. *anitratus* infections in an adult intensive care unit. *Am J Infect Control* 1990;18:288–291.
184. Corbella X et al. Emergence and rapid spread of carbapenem resistance during a large and sustained hospital outbreak of multiresistant *Acinetobacter baumannii*. *J Clin Microbiol* 2000;38:4086–4095.
185. Cox TR, Roland WE, Dolan ME. Ventilator-related *Acinetobacter* outbreak in an intensive care unit. *Mil Med* 1998;163:389–391.
186. Crowe M, Towner KJ, Humphreys H. Clinical and epidemiological features of an outbreak of acinetobacter infection in an intensive therapy unit. *J Med Microbiol* 1995;43:55–62.
187. D'Agata EM, Thayer V, Schaffner W. An outbreak of *Acinetobacter baumannii*: the importance of cross-transmission. *Infect Control Hosp Epidemiol* 2000;21:588–591.
188. French GL et al. A hospital outbreak of antibiotic-resistant *Acinetobacter anitratus*: epidemiology and control. *J Hosp Infect* 1980;1:125–131.
189. Go ES et al. Clinical and molecular epidemiology of acinetobacter infections sensitive only to polymyxin B and sulbactam. *Lancet* 1994;344:1329–1332.
190. Holton J. A report of a further hospital outbreak caused by a multi-resistant *Acinetobacter anitratus*. *J Hosp Infect* 1982;3:305–309.
191. Kapil A et al. Outbreak of nosocomial *Acinetobacter baumannii* bacteremia in a high risk ward. *Med Oncol* 1998;15:270–274.
192. Koeleman JG et al. Nosocomial outbreak of multi-resistant *Acinetobacter baumannii* on a surgical ward: epidemiology and risk factors for acquisition. *J Hosp Infect* 1997;37:113–123.
193. Levin AS et al. An outbreak of multiresistant *Acinetobacter baumannii* in a university hospital in San Paulo, Brazil. *Infect Control Hosp Epidemiol* 1996;17:366–368.
194. McDonald LC et al. Outbreak of *Acinetobacter* spp. bloodstream infections in a nursery associated with contaminated aerosols and air conditioners. *Pediatr Infect Dis J* 1998;17:716–722.
195. Pillay T et al. An outbreak of nosocomial infection with *Acinetobacter* linked to contaminated suction catheters. *J Hosp Infect* 1999;43:299–304.
196. Riley TV et al. Outbreak of gentamicin-resistant *Acinetobacter baumannii* in an intensive care unit: clinical, epidemiological and microbiological features. *Pathology* 1996;28:359–363.
197. Sakata H et al. *Acinetobacter calcoaceticus* biovar *anitratus* septicemia in a neonatal intensive care unit: epidemiology and control. *J Hosp Infect* 1989;14:15–22.

***Acinetobacter* spp.**

179. Allen KD, Green HT. Hospital outbreak of multi-resistant *Acinetobacter anitratus*: an airborne mode of spread? *J Hosp Infect* 1987;9:110–119.
180. Bernards AT et al. Methicillin-resistant *Staphylococcus aureus* and *Acinetobacter baumannii*: an unexpected difference in epidemiologic behavior. *Am J Infect Control* 1998;26:544–551.
181. Castle M et al. Outbreak of a multiply resistant *Acinetobacter* in a surgical intensive care unit: epidemiology and control. *Heart Lung* 1978;7:641–644.
182. Cefai C et al. An outbreak of *Acinetobacter* respiratory tract infection resulting from incomplete disinfection of ventilatory equipment. *J Hosp Infect* 1990;15:177–182.

198. Stone JW, Das BC. Investigation of an outbreak of infection with *Acinetobacter calcoaceticus* in a special care baby unit. *J Hosp Infect* 1986;7:42–48.
199. Struelens MJ et al. Nosocomial colonization and infection with multiresistant *Acinetobacter baumannii*: outbreak delineation using DNA macrorestriction analysis and PCR-fingerprinting. *J Hosp Infect* 1993;25:15–32.
200. Tankovic J et al. Characterization of a hospital outbreak of imipenem-resistant *Acinetobacter baumannii* by phenotypic and genotypic typing methods. *J Clin Microbiol* 1994;32:2677–2681.

Enteric pathogens

201. Adler JL et al. A protracted hospital-associated outbreak of salmonellosis due to a multiple-antibiotic-resistant strain of *Salmonella indiana*. *J Pediatr* 1970;77:970–975.
202. Alkan M, Soffer S. Emergence of resistance to antibiotics during an outbreak of hospital-acquired salmonellosis. *J Hosp Infect* 1982;3:185–187.
203. Barnass S et al. The tangible cost implications of a hospital outbreak of multiply-resistant *Salmonella*. *Epidemiol Infect* 1989;103:227–234.
204. Buch NA, Dhananjiya A. A nursery outbreak of multidrug resistant *Salmonella typhimurium*. *Indian Pediatr* 1998;35:455–459.
205. Hammami A et al. Nosocomial outbreak of acute gastroenteritis in a neonatal intensive care unit in Tunisia caused by multiply drug resistant *Salmonella wien* producing SHV-2 beta-lactamase. *Eur J Clin Microbiol Infect Dis* 1991;10:641–646.
206. Joseph AT et al. *Salmonella senftenberg* outbreak in a neonatal unit. *Indian Pediatr* 1990;27:157–160.
207. Kumar A et al. An outbreak of multidrug resistant *Salmonella typhimurium* in a nursery. *Indian Pediatr* 1995;32:881–885.
208. Lamb VA et al. Outbreak of *Salmonella typhimurium* gastroenteritis due to an imported strain resistant to ampicillin, chloramphenicol, and trimethoprim-sulfamethoxazole in a nursery. *J Clin Microbiol* 1984;20:1076–1079.
209. Mahajan R et al. Nosocomial outbreak of *Salmonella typhimurium* infection in a nursery intensive care unit and paediatric ward. *J Commun Dis* 1995;27:10–14.
210. McCall B et al. An outbreak of multi-resistant *Shigella sonnei* in a long-stay geriatric nursing centre. *Commun Dis Intell* 2000;24:272–275.
211. Newman MJ. Multiple-resistant *Salmonella* group G in a neonatal intensive care unit. *West Afr J Med* 1996;15:165–169.
212. Pillay DG et al. Nosocomial transmission of *Shigella dysenteriae* type 1. *J Hosp Infect* 1997;37:199–205.
213. Robins-Browne RM et al. A hospital outbreak of multiresistant *Salmonella typhimurium* belonging to phage type 193. *J Infect Dis* 1983;147:210–216.

Mycobacterium tuberculosis

214. Agerton T et al. Transmission of a highly drug-resistant strain (strain W1) of *Mycobacterium tuberculosis*. Community outbreak and nosocomial transmission via a contaminated bronchoscope. *JAMA* 1997;278:1073–1077.
215. Bouvet E et al. A nosocomial outbreak of multidrug-resistant *Mycobacterium bovis* among HIV-infected patients. A case-control study. *AIDS* 1993;7:1453–1460.
216. Breathnach AS et al. An outbreak of multi-drug-resistant tuberculosis in a London teaching hospital. *J Hosp Infect* 1998;39:111–117.
217. Hannan MM et al. Investigation and control of a large outbreak of multi-drug resistant tuberculosis at a central Lisbon hospital. *J Hosp Infect* 2001;47:91–97.
218. Kenyon TA et al. A nosocomial outbreak of multidrug-resistant tuberculosis. *Ann Intern Med* 1997;127:32–36.
219. Moro ML et al. Effectiveness of infection control measures in controlling a nosocomial outbreak of multidrug-resistant tuberculosis among HIV patients in Italy. *Int J Tuberc Lung Dis* 2000;4:61–68.
220. Rivero A et al. High rate of tuberculosis reinfection during a nosocomial outbreak of multidrug-resistant tuberculosis caused by *Mycobacterium bovis* strain B. *Clin Infect Dis* 2001;32:159–161.
221. Stroud LA et al. Evaluation of infection control measures in preventing the nosocomial transmission of multidrug-resistant *Mycobacterium tuberculosis* in a New York City hospital. *Infect Control Hosp Epidemiol* 1995;16:141–147.
222. Wenger PN et al. Control of nosocomial transmission of multidrug-resistant *Mycobacterium tuberculosis* among healthcare workers and HIV-infected patients. *Lancet* 1995;345:235–240.

Other

223. de Galan BE et al. Hospital-related outbreak of infection with multidrug-resistant *Streptococcus pneumoniae* in the Netherlands. *J Hosp Infect* 1999;42:185–192.
224. Gould FK, Magee JG, Ingham HR. A hospital outbreak of antibiotic-resistant *Streptococcus pneumoniae*. *J Infect* 1987;15:77–79.

225. Hazuka BT et al. Two outbreaks of *Flavobacterium septicum* type E in a neonatal intensive care unit. *J Clin Microbiol* 1977;6:450–455.
226. Hekker TA et al. A nosocomial outbreak of amoxicillin-resistant non-typable *Haemophilus influenzae* in a respiratory ward. *J Hosp Infect* 1991; 19:25–31.
227. Millar MR et al. Outbreak of infection with penicillin-resistant *Streptococcus pneumoniae* in a hospital for the elderly. *J Hosp Infect* 1994;27:99–104.
228. Nuorti JP et al. An outbreak of multidrug-resistant pneumococcal pneumonia and bacteremia among unvaccinated nursing home residents. *N Engl J Med* 1998;338:1861–1868.
229. Oppenheim BA et al. Outbreak of coagulase negative staphylococcus highly resistant to ciprofloxacin in a leukaemia unit. *BMJ* 1989;299:294–297.
230. Orth B et al. Outbreak of invasive mycoses caused by *Paecilomyces lilacinus* from a contaminated skin lotion. *Ann Intern Med* 1996;125:799–806.
231. Patterson JE et al. A nosocomial outbreak of ampicillin-resistant *Haemophilus influenzae* type b in a geriatric unit. *J Infect Dis* 1988;157:1002–1007.
232. Purvis RS, Tyring SK. An outbreak of lindane-resistant scabies treated successfully with permethrin 5% cream. *J Am Acad Dermatol* 1991; 25: 1015–1016.
233. Quinn JP et al. Outbreak of JK diphtheroid infections associated with environmental contamination. *J Clin Microbiol* 1984;19:668–671.
234. Reboli AC et al. An outbreak of *Burkholderia cepacia* lower respiratory tract infection associated with contaminated albuterol nebulization solution. *Infect Control Hosp Epidemiol* 1996;17:741–743.