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

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Contents

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 community 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
Staphylococcus aureus	methicillin vancomycin
Staphylococcus epidermidis	vancomycin
Enterococci	aminoglycoside (high level) ampicillin vancomycin
Streptococcus pneumoniae	penicillin
Enterobacteriaceae	aminoglycosides third-generation cephalosporins monobactams ceftazidime
Pseudomonas aeruginosa	fluoroquinolones extended-spectrum penicillins fluoroquinolones aminoglycosides ceftazidime carbapenems
Acinetobacter spp	aminoglycosides ceftazidime carbapenems
Mycobacterium tuberculosis	isoniazid rifampin streptomycin ethambutol pyrazinamide
Candida spp	amphotercin b azoles
Herpes simplex	acycolvir
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, infections 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, multifaceted 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 Semmelweiss (*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. Similarily, 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 marcesens*, *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 aminoglycolide-resistant Gram-negative organisms with environmental interventions alone (*79*). A high concentration of these organisms was present in the standing water for cut plants. Removal of plants and water, together with daily dry mopping, was temporally 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 postoperative 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 respiratory 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 infection 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 infection 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.

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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]
								Screening									
		Hand hygiene	Barriers	Cohort	Education	Environment	Other[3]	Patient	Staff	Environment	Epidemiological typing	Colonized patients	Colonized staff	Restriction	Guidelines		
Methicillin-resistant *S. aureus*																	
Alonso 1997 (1)	10/5		+			+		+	+		+	+					Eradicated
Alvarez 1985 (2)	11	+	+	+	+			+	+		+						Controlled
Andersen 1999 (3)	5/5	+	+			+		+	+		+						Eradicated initially; reintroduced
Arnow 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]
								Screening									
		Hand hygiene	Barriers	Cohort	Education	Environment	Other[2]	Patient	Staff	Environment	Epidemiological typing	Colonized patients	Colonized staff	Restriction	Guidelines		
Methicillin-resistant *S. aureus (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]
								Screening									
		Hand hygiene	Barriers	Cohort	Education	Environment	Other[3]	Patient	Staff	Environment	Epidemiological typing	Colonized patients	Colonized staff	Restriction	Guidelines		
Methicillin-resistant *S. aureus (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]
								Screening									
		Hand hygiene	Barriers	Cohort	Education	Environment	Other[2]	Patient	Staff	Environment	Epidemiological typing	Colonized patients	Colonized staff	Restriction	Guidelines		
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
Livornese 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]
								Screening									
		Hand hygiene	Barriers	Cohort	Education	Environment	Other[3]	Patient	Staff	Environment	Epidemiological typing	Colonized patients	Colonized staff	Restriction	Guidelines		
Enterobacteriaceae *(cont'd)*																	
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]
								Screening									
		Hand hygiene	Barriers	Cohort	Education	Environment	Other[3]	Patient	Staff	Environment	Epidemiological typing	Colonized patients	Colonized staff	Restriction	Guidelines		
Enterobacteriaceae *(cont'd)*																	
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]
								Screening									
		Hand hygiene	Barriers	Cohort	Education	Environment	Other[3]	Patient	Staff	Environment	Epidemiological typing	Colonized patients	Colonized staff	Restriction	Guidelines		
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]
								Screening									
		Hand hygiene	Barriers	Cohort	Education	Environment	Other[2]	Patient	Staff	Environment	Epidemiological typing	Colonized patients	Colonized staff	Restriction	Guidelines		
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]
								Screening									
		Hand hygiene	Barriers	Cohort	Education	Environment	Other[3]	Patient	Staff	Environment	Epidemiological typing	Colonized patients	Colonized staff	Restriction	Guidelines		
Enteric pathogens *(cont'd)*																	
Lamb 1984 (208)	5	+	+					+	+	+	+						Eradicated
Mahajan 1995 (209)	48		+			+			+	+						Suction machines	Eradicated
McCall[2] 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 (*S. pneumoniae*)
Gould 1987 (224)	5/1							+	+			+					Eradicated (*S. pneumoniae*)
Hazuka 1977 (225)	3/7		+	+		+	UC	+	+	+							Eradicated (*Flavobacterium meningosepticum*)
Hekker 1991 (226)	13		+	+				+	+		+	+	+				Eradicated (H. influenzae)
Millar 1994 (227)	15	+					Restrict mobility	+	+								Eradicated (S. pneumoniae)
Nuorti 1998 (228)	11/17						Vaccine	+	+		+				+		Controlled (*S. pneumoniae*)
Oppenheim 1989 (229)	21				+			+	+	+	+	+		+	+		Eradicated (coagulase-negative Staphylococci)
Orth 1996 (230)	12					+	UC		+	+						Topical moisturizer	Eradicated (*Paecilomyces lilacinus*)

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

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