

Isolation measures in the hospital management of methicillin resistant *Staphylococcus aureus* (MRSA): systematic review of the literature

B S Cooper, S P Stone, C C Kibbler, B D Cookson, J A Roberts, G F Medley, G Duckworth, R Lai, S Ebrahim

Abstract

Objective To evaluate the evidence for the effectiveness of isolation measures in reducing the incidence of methicillin resistant *Staphylococcus aureus* (MRSA) colonisation and infection in hospital inpatients.

Design Systematic review of published articles.

Data sources Medline, Embase, CINAHL, Cochrane Library, System for Information on Grey Literature in Europe (SIGLE), and citation lists (1966-2000).

Review methods Articles reporting MRSA related outcomes and describing an isolation policy were selected. No quality restrictions were imposed on studies using isolation wards or nurse cohorting. Other studies were included if they were prospective or employed planned comparisons of retrospective data.

Results 46 studies were accepted; 18 used isolation wards, nine used nurse cohorting, and 19 used other isolation policies. Most were interrupted time series, with few planned formal prospective studies. All but one reported multiple interventions. Consideration of potential confounders, measures to prevent bias, and appropriate statistical analysis were mostly lacking. No conclusions could be drawn in a third of studies. Most others provided evidence consistent with a reduction of MRSA acquisition. Six long interrupted time series provided the strongest evidence. Four of these provided evidence that intensive control measures including patient isolation were effective in controlling MRSA. In two others, isolation wards failed to prevent endemic MRSA.

Conclusion Major methodological weaknesses and inadequate reporting in published research mean that many plausible alternative explanations for reductions in MRSA acquisition associated with interventions cannot be excluded. No well designed studies exist that allow the role of isolation measures alone to be assessed. None the less, there is evidence that concerted efforts that include isolation can reduce MRSA even in endemic settings. Current isolation measures recommended in national guidelines should continue to be applied until further research establishes otherwise.

Introduction

The incidence of hospital acquired methicillin resistant *Staphylococcus aureus* (MRSA) continues to rise globally.¹⁻⁴ Attempts to control this spread have relied principally on three measures: hand hygiene among healthcare workers, restriction of antibiotics, and the detection and isolation of infected or colonised patients. We consider the detection and isolation of infected or colonised patients, which is central to most national guidelines.⁵⁻⁸

Isolation measures for patients are intended to interrupt transmission of MRSA. The most intensive forms of isolating patients are isolation wards (designated for the treatment of known or suspected carriers of MRSA) and nurse cohorting (the physical segregation of MRSA patients in one part of a ward, with nursing by designated staff who care exclusively for these patients). Other isolation measures include the use of single bedded rooms, cohorts of patients on general wards (without designated nursing staff), and barrier precautions (use of aprons or gowns, gloves, and, in some cases, masks by healthcare workers as the only physical barrier to transmission).

Such control measures may place substantial burdens on hospital resources, and the value of their continued use has been questioned⁹ but the effectiveness of isolation measures in reducing transmission and controlling MRSA has not been assessed systematically. Much of the research is of a quasi-experimental nature^{8, 10} and the associated threats to validity need to be considered.^{11, 12} We therefore undertook a systematic review of the evidence for the effectiveness of isolation measures in the management of MRSA in hospitals.

Method

Search strategy

We developed a search strategy that covers the main subject areas of the review (MRSA, screening, and isolation of patients and control of infection). We searched the following databases, with no language restrictions: Medline 1966-December 2000, Embase 1980-December 2000, CINAHL 1982-May 2000, System for

University
Department
Medical
Microbiology, Royal
Free Campus, Royal
Free and University
College Medical
School, University
London, London
NW3 2PF]

B S Cooper
*postdoctoral research
fellow*

C C Kibbler
*postdoctoral research
fellow*

Academic
Department
Geriatric Medicine,
Royal Free Campus,
Royal Free and
University College
Medical School
S P Stone
senior lecturer

Laboratory of
Healthcare
Associated
Infection, Central
Public Health,
Laboratory, Health
Protection Agency,
London NW9 5HT

B D Cookson
director

Collaborative
Centre for
Economics of
Infectious Disease,
Department Public
Health and Policy,
London School of
Hygiene and
Tropical Medicine,
University London
WC1E 7HT

J A Roberts
*professor in economics
of infectious disease*

Department of
Biological Sciences,
University of
Warwick, Coventry
CV4 7AL UK
G F Medley
*reader, ecology and
epidemiology*

continued over



This is an abridged version, the long version is on bmj.com

BMJ 2004;329:533-9

Division of
Healthcare
Associated Infection
and Antimicrobial
Resistance, Health
Protection Agency,
Communicable
Disease
Surveillance Centre,
London NW9 5EQ
G Duckworth
director

University Library,
Royal Free Campus,
Royal Free and
University College
Medical School
R Lai
assistant librarian

Department of
Social Medicine,
Bristol University
Medical School,
University of Bristol
BSS 2PR
S Ebrahim
*professor in
epidemiology of
ageing*

Correspondence to:
S P Stone s.stone@
rfc.ucl.ac.uk

Information on Grey Literature in Europe (SIGLE) 1980-May 2000, and the *Cochrane Library* to December 2000. We also hand searched key journals.

Study selection

Articles were obtained if abstracts mentioned endemic or epidemic MRSA and an attempt at control in hospital. As the number of studies was far greater than anticipated, we revised the original protocol (which had imposed no quality restrictions). We imposed the minimal requirement that accepted studies should include a component of prospective data collection. If they were entirely retrospective comparisons should have been planned and not prompted by part of the outcome data. No such restrictions were imposed for studies using the most intensive forms of isolation (isolation wards and nurse cohorting) as these have the greatest implications for the allocation of resources and organisation of services. We rejected studies not mentioning an isolation policy or without relevant MRSA related outcomes.

Data extraction

We divided each study into phases, where appropriate, defined by major changes in isolation or other infection control measure. Data extraction included documentation of potential threats to validity, measures taken to avoid, record, or adjust for these and an assessment of the appropriateness of any statistical analysis undertaken.

Data synthesis

Two reviewers independently evaluated the strength of evidence in each study by examining the study design, quality of data, and presence of plausible alternative explanations of outcomes. They characterised the evidence on a case by case basis as “none,” “weak,” “of intermediate strength,” or “stronger.” We considered formal meta-analysis inappropriate because of heterogeneity in outcome measures and patient populations. Full details of the search strategy, study selection, and data extraction are available in a technical report.¹³

Results

The search selected 4382 abstracts. Appraisal of abstracts selected 254 papers. The final review included 46 studies (table 1).¹⁴⁻⁶⁰

Table 1 Characteristics of the 46 accepted studies

Highest level of isolation	Isolation ward	Nurse cohorting	Other isolation measures
No of studies	18	9	19
Range of study durations	3 months-15 years	3.5 months-4 years	1 month-9 years
Whole hospital setting	16	3	7
Hospital unit setting (such as burns, intensive care)	2	6	12
Other control measures			
Screening for MRSA	18	9	14
Topical eradication therapy	12	5	8
Hand hygiene programme	8	2	6
Antibiotic restriction	3	0	2
Study design			
Prospective interrupted time series	1	2	8
Retrospective interrupted time series	15	3	2
Hybrid retrospective and prospective interrupted time series	0	2	5
Retrospective cohort study	0	0	1
Non-comparative (one phase) studies	2	2	3

Study design

We found no randomised controlled trials and only four prospective planned comparison studies with pre-defined study phases.^{19 37 49 60} Most designs were interrupted time series—that is, time series of outcome measures recorded before and after one or more interventions.

Review of the 36 studies allowing comparisons between isolation policies indicated that in 27 the comparisons being made were dependent on knowledge of the outcome data. Short retrospective studies with successful outcomes were particularly vulnerable to this problem. This, and the predominance of unplanned retrospective reports, shows that reporting bias is likely to be important.

Threats to internal validity of evidence

In the absence of cluster randomised trials, all comparative studies were vulnerable to selection bias, yet recording and adjustment of potential confounders was minimal (table 2). In two studies we considered changes in case mix to represent a plausible explanation for changes in the incidence of MRSA.^{40 43}

Table 2 details other important biases, the studies that were vulnerable to them (the majority) and the measures some took to avoid them (the minority).

Trends, regression to the mean, seasonal effects and changes in MRSA strain

Of 30 studies with two or more phases and pre-intervention time series, clear underlying trends in MRSA levels were apparent in 13. In all cases the trend was for increasing MRSA levels before major interventions.

Trends in the number of patients colonised on admission may also complicate interpretation of outcomes. Although 18 studies assessed whether patients were colonised on admission, we could only assess trends in five.^{29 30 37 45 47} In two studies these trends provided a plausible explanation for changes in outcome measures.^{29 43}

Regression to the mean effects were considered likely when unusually high MRSA incidence data prompted the intervention and when these data were included in the study. We considered this threat to provide a plausible explanation of outcomes in seven studies.^{15 19 20 21 44 45 55}

Inspection showed that seasonal effects may have been important in two^{20 55} of 14 studies with time series of 18 months or more. In the 21 studies with shorter time series it was not possible to disentangle seasonal from intervention effects. Although studies often gave no details of MRSA strain typing, we considered the documented introduction of a new strain to plausibly explain control failure.²⁹

Statistical validity

Of the 38 interrupted time series, 24 reported results of statistical analysis. In all but one study³⁵ patient outcomes were assumed by authors to be independent. Such assumptions are inappropriate when transmission from patient to patient occurs and would increase the likelihood of a false positive outcome. In one study we considered the independence assumption to be justified as outcomes at hospital level from distinct hospitals were used.²⁷

Table 2 Selection, performance, detection and attrition bias

Type of bias	Cause	Studies vulnerable	Measures taken to identify or prevent bias
Selection bias	Differences in intervention groups on study entry	Studies without randomisation (39 studies)	Four of 35 interrupted time series studies where isolation or screening changed presented data allowing comparisons of patient characteristics between phases ^{23 31 37 54} Two described unquantified changes in case mix. ^{41 43} One study presented partial adjustment for confounders ²⁷
Performance bias	Differences in care for patients between treatment groups, apart from interventions under investigation	Studies where specified aspect of care was not under investigation:	
	Differences in antibiotic prescribing	31 interrupted time series studies	Four presented details of antibiotic use. ^{15 19 33 60} Two alluded to unquantified changes ^{41 49}
	Differences in lengths of stay	29 interrupted time series studies	Changes in length of stay could be assessed in four ^{30 33 44 58}
	Differences in bed occupancy and staff workload	31 interrupted time series studies	Comparisons of bed occupancy between phases possible in four. ^{15 21 44 55} Changes in staffing levels or workloads could be assessed in five. ^{15 21 23 29 44}
Detection bias	Differential outcome assessment between intervention groups:	All studies:	Three reported some blinding of outcome assessors ^{31 43 54}
	Differences in diagnosis of infections	26 studies	16 specified diagnostic criteria. 14 reported MRSA bacteraemias
	Differences in screening practices	10 studies with colonisation data only	In all cases screening effort either reported not to have changed or to have changed in opposite direction from outcomes, suggesting screening effort could not explain the changes
Attrition bias	Differential loss to follow up between treatment groups. Since hospital acquired infections may first become apparent after discharge, changes to length of stay could lead to attrition bias	Studies where outcomes are infections (26 studies) and with substantial changes in length of stay	None: no studies followed up patients after discharge to detect hospital acquired infections

Evidence for control of MRSA

In 45 of the 46 studies multiple simultaneous control measures were apparent. It was not possible to assess the relative contribution of individual measures.

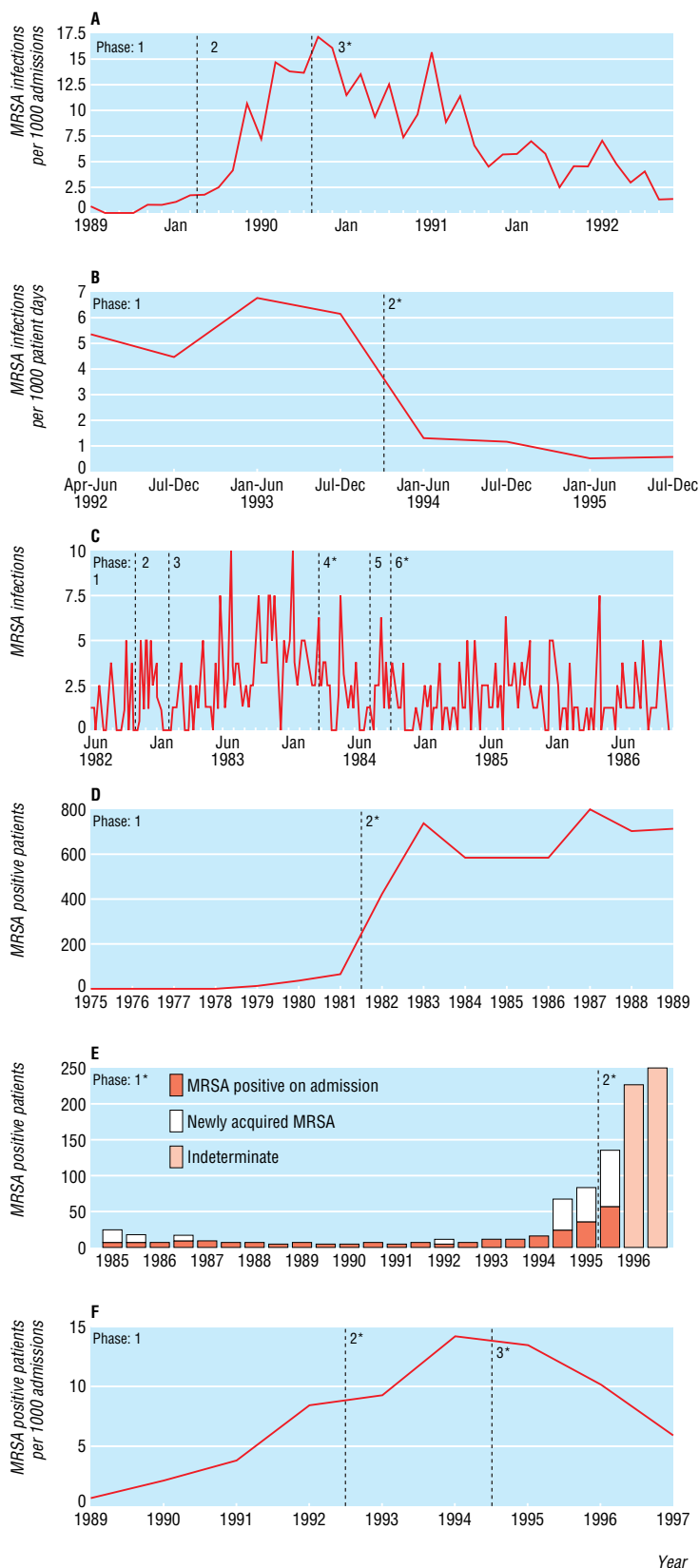
In 14 studies it was impossible to draw any conclusions about the effect of interventions. Most of the remaining 32 reported evidence consistent with reduction in MRSA transmission but in 18 of these the evidence was considered weak, especially in small and successfully controlled outbreaks managed by isolation

wards or nurse cohorting.^{14 16 36 47 48 50 52 53 58} None the less, it remains possible that immediate deployment of such measures may be successful.

The strongest evidence came from six longer time series, with detailed information on interventions and fewer plausible alternative explanations for the outcome (table 3, figure). In four studies major outbreaks were controlled or MRSA numbers substantially reduced over prolonged periods.^{22 23 25 32 33} The main isolation measures were single room in two

Table 3 Studies providing stronger evidence

Study	Setting and study population	Design	Main interventions	Patient outcomes	Assessment of evidence
Coello et al, 1994 ²²	Teaching hospital 1500 beds	Prospective interrupted time series. Three phases: 8, 8, and 26 months	Phases 1 and 2: minimal isolation and screening Phase 3: single room isolation and nurse cohorting, contact screening, prompt discharge of MRSA cases Topical eradication of MRSA carriage with neomycin nasal cream in phase 1 and with mupirocin in phases 2 and 3	Figure: A 476 infected patients throughout	Evidence that a major outbreak was controlled by combined interventions. Lacks information on many potential confounders
Cosseron-Zerbib et al, 1998 ²³	Paediatric ICU 20 beds	Hybrid retrospective and prospective interrupted time series. Two phases: 21 and 24 months.	Phase 1: screening for last 11 months Phase 2: single room isolation, cohorting, screening, feedback, handwashing education, barrier nursing, chlorhexidine soap, and other measures	Figure: B MRSA infections: Phase 1: 50 Phase 2: 6	Evidence that interventions reduced MRSA infections. Regression to mean and Hawthorne effects supply less plausible alternative explanations
Duckworth et al 1988, ²⁵	Teaching hospital 645 beds	Retrospective interrupted time series. Six phases: 4, 3, 13.5, 4, 1.5, 26 months	Initial isolation: mainly single rooms and some cohorting (phases 1-3), changing to mainly isolation ward (phases 4-6). Simultaneous changes to screening, eradication and other measures	Figure: C 408 MRSA infections throughout	Evidence supporting efficacy of combined measures in reducing incidence. Many potential confounders not recorded
Faoagali et al, 1992 ²⁸	Teaching hospital 1200 beds	Retrospective interrupted time series. Two phases: 7 and 8 years	Isolation ward throughout Phase 1: minimal overflow from isolation ward Phase 2: overflow isolated in single rooms Additional measures in phase 2 include: pre-screening of admissions and transfers in; handwashing education; antibiotic restriction	Figure: D	Evidence that combined measures in both phases failed to prevent MRSA spreading and becoming endemic
Farrington et al, 1998 ²⁹	Teaching hospital 1000 beds	Retrospective interrupted time series. Two phases: 9.5 and 2.5 years	Continual operation of isolation ward Phase 1: minimal overflow from isolation ward Phase 2: overflow cohorted and isolated in single rooms Screening, ward closure and eradication policies relaxed slightly in phase 2	Figure: E 221 MRSA acquisitions, 206 colonised on admission, 61 uncertain	Evidence supporting control of MRSA for 9.5 years by combined measures followed by eventual control failure related to rise in numbers colonised on admission or to change in strain rather than changed control measures
Harbath et al, 2000, ³² Pittet et al, 2000 ³³	Teaching hospital 1300-1600 beds	Hybrid retrospective and prospective interrupted time series. Three phases: 4, 2, and 3 years	Phase 1: No control measures Phase 2: Single room isolation, screening, mupirocin Phase 3: as phase 2 + hand hygiene, education, and feedback programme	Figure: F 1771 MRSA colonisations and infections. 158 bacteraemias	Evidence supporting control by combined interventions Some potential confounders, but these provide less plausible explanations for the changes



Outcome of studies considered to present the strongest evidence Interrupted time series for A: Coello et al²² B: Cosseron Zerbib et al²³ C: Duckworth et al²⁵ D: Faoagli et al²⁸ E: Farrington et al²⁹ F: Harbath et al.^{32, 33} Table 3 gives explanatory text. Asterisks indicate phases with most intensive isolation policies. In D and E isolation policies in both phases were similar (isolation wards), but in the second phase the capacities of the isolation wards were exceeded in both cases, and the overflow was cohorted or isolated in single rooms

studies,^{23 32 33} nurse cohorting in one,²² and isolation ward in one.²⁵ Another isolation ward study reported failure to control the spread of MRSA,²⁸ and another reported control by an isolation ward for many years followed by eventual failure.²⁹

We considered eight other studies to present “intermediate” evidence of reduction of MRSA by measures that included an isolation ward,^{13 51} nurse cohorting,^{15 19} or other interventions.^{27 35 37} One showed the failure of an isolation ward to control MRSA.²⁴

Discussion

Our primary conclusion is that major methodological weaknesses and inadequate reporting in research into the effectiveness of isolation measures mean that many plausible alternative explanations for reductions in MRSA cannot be excluded. We have produced guidelines to facilitate the planning and publication of better quality studies.¹³

The secondary conclusion is that, despite the limitations of existing research we found evidence that concerted interventions that include isolation measures can reduce MRSA transmission substantially, even in settings with endemic MRSA. We found no evidence to show that current isolation measures recommended in many countries⁵⁻⁸ are ineffective at reducing transmission from isolated patients: the only two studies that directly measured this reported large reduction in the transmission rate per source.^{27 35} None the less, we found reports of control failure despite the employment of intensive isolation measures including isolation wards.^{28 29} These studies indicate a need to investigate precisely how such isolation measures should be used. We address this question further elsewhere, using mathematical models to explore the effectiveness and cost effectiveness of isolation wards under different assumptions.^{13 61}

Strengths of the study

In contrast with narrative reviews,^{3 10 62 63 64-66} where study selection may be biased, our systematic comprehensive search strategy, data extraction and documentation of component threats to validity provided a rigorous evaluation of the shortcomings of existing research. In particular, no studies tell us anything about the relative effectiveness or cost effectiveness of individual measures in different clinical situations. These would be fertile areas for further research.

Nevertheless, a lack of evidence of an effect associated with specific measures should not be mistaken for evidence of lack of effect. Having considered the evidence we believe isolation measures recommended in national guidelines should continue until further research establishes otherwise.

The six studies^{19 20 22 25 26 29 30} we considered to present the strongest evidence for assessing the effect of isolation, although they often failed to consider potentially important confounders, provide testable hypotheses that could be assessed in future studies.

What is already known on this topic

National guidelines in many countries recommend patient isolation to control the spread of MRSA

Traditional narrative reviews differ as to its effectiveness

Most of the research is of a quasi-experimental nature, and no review has systematically assessed the threats to valid inference associated with such studies

What this study adds

The shortcomings of existing research are rigorously evaluated through a systematic comprehensive search strategy, data extraction, and documentation of component threats to validity

Major methodological weaknesses and inadequate reporting in many studies mean that plausible alternative explanations for reductions in MRSA cannot be excluded

There is evidence that interventions that include isolation can achieve major reductions in MRSA, even when endemic, but there are no well designed studies that allowed the role of isolation measures alone to be assessed

Studies considered to provide stronger evidence or evidence of intermediate strength provide testable hypotheses for future well planned studies

Guidelines have been produced to facilitate such research (www.hta.nhsweb.nhs.uk)

Priority for research

MRSA is associated with substantial morbidity and mortality.^{8 67} The emergence of glycopeptide resistant *Staphylococcus aureus* strains,⁶⁸ which further reduce therapeutic options, makes the implementation of well designed interventional studies to inform the choice of control measures a research priority.

The study was funded for two years by the Health Technology Assessment Board of the NHS R&D HTA Programme.

Competing interests: None declared.

- Public Health Laboratory Service. The first year of the Department of Health's mandatory MRSA bacteraemia surveillance scheme in acute NHS trusts in England: April 2001-March 2002. *Commun Dis Rep CDR Wkly* [serial online] 2002;12: www.hpa.org.uk/cdr/PDFfiles/2002/cdr2502.pdf (accessed 22 Jul 2004).
- Hiramatsu K, Hanaki H, Ino T. Methicillin resistant *Staphylococcus aureus* clinical strain with reduced vancomycin susceptibility. *J Antimicrob Chemother* 1997;40:135-6.
- Turnidge JD, Bell JM. Methicillin-resistant *Staphylococcus aureus* evolution in Australia over 35 years. *Microb Drug Resist* 2000;6:223-9.
- Centers for Disease Control and Prevention. National nosocomial infection surveillance systems report, data summary from January 1992-June 2001, issued August 2001. *Am J Infect Control* 2002;30:458-75.
- Garner JS. Hospital infection control practices advisory committee. Guideline for isolation precautions in hospitals. *Infect Control Hosp Epidemiol* 1996;17:53-80.
- Wierkgroup Infectie Preventie. *Management policy for methicillin-resistant Staphylococcus aureus*. Guideline No. 35A. Leiden: WIP, 1994.
- Ministry of Health. *Guidelines for the control of methicillin-resistant Staphylococcus aureus in New Zealand*. Wellington: MoH, 2002. [www.moh.govt.nz/moh.nsf/49ba80c00757b8804c256673001d47d0/e5231b74a5dc8b22c56220017b248/\\$FILE/mrsa.pdf](http://www.moh.govt.nz/moh.nsf/49ba80c00757b8804c256673001d47d0/e5231b74a5dc8b22c56220017b248/$FILE/mrsa.pdf) (accessed 12 Jul 2004).
- British Society for Antimicrobial Chemotherapy, Hospital Infection Society and the Infection Control Nurses Association. Revised guidelines for the control of methicillin-resistant *Staphylococcus aureus* infection in hospitals. *J Hosp Infect* 1998;39:253-90.
- Rahman M, Sanderson PJ, Bentley AH, Barrett SP, Karim QN, Teare EL, et al. Control of MRSA. *J Hosp Infect* 2000;44:151-3.
- Stone SP. Managing methicillin-resistant *Staphylococcus aureus* in hospital: the balance of risk. *Age Ageing* 1997;26:165-8.
- Cook TD, Campbell DT. *Quasi-experimentation: design and analysis issues for field settings*. Chicago: Rand McNally College Publications, 1979.
- The Cochrane Effective Practice and Organisation of Care (EPOC) Review Group. Cochrane Library Database. Oxford: Update software; Issue 1 2001.
- Cooper BS, Stone SP, Kibbler CC, Cookson BD, Roberts JA, Medley GF, Duckworth GJ, Lai R, Ebrahim S. Systematic review of isolation policies in the hospital management of methicillin-resistant *Staphylococcus aureus*: a review of the literature with epidemiological and economic modelling. *Health Technol Assess* 2003;7:1-194.
- Alvarez S, Shell C, Gage K, Guarderas J, Kasprzyk D, Besing J, et al. An outbreak of methicillin-resistant *Staphylococcus aureus* eradicated from a large teaching hospital. *Am J Infect Control* 1985;13:115-21.
- Arnoff P, Allyn PA, Nichols EM, Hill DL, Pezzlo M, Bartlett RH. Control of methicillin-resistant *Staphylococcus aureus* in a burn unit: role of nurse staffing. *J Trauma* 1982;22:954-9.
- Back NA, Linnemann CC, Jr, Staneck JL, Kotagal UR. Control of methicillin-resistant *Staphylococcus aureus* in a neonatal intensive-care unit: use of intensive microbiologic surveillance and mupirocin. *Infect Control Hosp Epidemiol* 1996;17:227-31.
- Barakate MS, Harris JP, West RH, Vickery AM, Sharp CA, Macleod C, et al. A prospective survey of current methicillin-resistant *Staphylococcus aureus* control measures. *Austr N Z J Surg* 1999;69:712-6.
- Barakate MS, Yang YX, Foo SH, Vickery AM, Sharp CA, Fowler LD, et al. An epidemiological survey of methicillin-resistant *Staphylococcus aureus* in a tertiary referral hospital. *J Hosp Infect* 2000;44:19-26.
- Blumberg LH, Klugman KP. Control of methicillin-resistant *Staphylococcus aureus* bacteraemia in high-risk areas. *Eur J Clin Microbiol Infect Dis* 1994;13:82-5.
- Brady LM, Thomson M, Palmer MA, Harkness JL. Successful control of endemic MRSA in a cardiothoracic surgical unit. *Med J Austr* 1990;152:240-5.
- Campbell JR, Zaccaria E, Mason EO Jr, Baker CJ. 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.
- Coello R, Jimenez J, Garcia M, Arroyo P, Minguez D, Fernandez C, et al. Prospective study of infection, colonization and carriage of methicillin-resistant *Staphylococcus aureus* in an outbreak affecting 990 patients. *Eur J Clin Microbiol Infect Dis* 1994;13:74-81.
- Cosseron-Zerbib M, Roque Afonso AM, Naas T, Durand P, Meyer L, Costa et al. A control programme for MRSA (methicillin-resistant *Staphylococcus aureus*) containment in a paediatric intensive care unit: evaluation and impact on infections caused by other micro-organisms. *J Hosp Infect* 1998;40:225-35.
- Cox RA, Conquest C, Mallaghan C, Marples RR. A major outbreak of methicillin-resistant *Staphylococcus aureus* caused by a new phage-type (EMRSA-16). *J Hosp Infect* 1995;29:87-106.
- 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.
- El Hagrasy M. An outbreak of methicillin-resistant *Staphylococcus aureus* (MRSA) in a hospital in the UAE: Problems and solutions. *Emirates Med J* 1997;15:17-21.
- Esveld MI, de Boer AS, Notenboom AJ, van Pelt W, van Leeuwen WJ. [Secondary infection with methicillin resistant *Staphylococcus aureus* in Dutch hospitals (July 1994-June 1996)]. *Nederlands Tijdschrift voor Geneeskunde* 1999;143:205-8.
- Faoagali JL, Thong ML, Grant D. Ten years' experience with methicillin-resistant *Staphylococcus aureus* in a large Australian hospital. *J Hosp Infect* 1992;20:113-9.
- Farrington M, Redpath C, Trundle C, Coomber S, Brown NM. Winning the battle but losing the war: methicillin-resistant *Staphylococcus aureus* (MRSA) at a teaching hospital. *QJM* 1998;91:539-48.
- Girou E, Pujade G, Legrand P, Cizeau F, Brun-Buisson C. Selective screening of carriers for control of methicillin-resistant *Staphylococcus aureus* (MRSA) in high-risk hospital areas with a high level of endemic MRSA. *Clin Infect Dis* 1998;27:543-50.
- Girou E, Azar J, Wolkenstein P, Cizeau F, Brun-Buisson C, Roujeau JC. Comparison of systematic versus selective screening for methicillin-resistant *Staphylococcus aureus* carriage in a high-risk dermatology ward. *Infect Control Hosp Epidemiol* 2000;21:583-7.
- Harbarth S, Martin Y, Rohner P, Henry N, Auckenthaler R, Pittet D. Effect of delayed infection control measures on a hospital outbreak of methicillin-resistant *Staphylococcus aureus*. *J Hosp Infect* 2000;46:43-9.
- Pittet D, Hugonnet S, Harbarth S, Mourouga P, Sauvan V, Touveneau S, et al. Effectiveness of a hospital-wide programme to improve compliance with hand hygiene. Infection Control Programme. *Lancet* 2000;356:1307-12.
- Hartstein AI, LeMonte AM, Iwamoto PK. DNA typing and control of methicillin-resistant *Staphylococcus aureus* at two affiliated hospitals. *Infect Control Hosp Epidemiol* 1997;18:42-8.
- Jernigan JA, Titus MG, Groschel DH, Getchell-White S, Farr BM. Effectiveness of contact isolation during a hospital outbreak of methicillin-resistant *Staphylococcus aureus*. *Am J Epidemiol* 1996;143:496-504.
- Jones MR, Martin DR. Outbreak of methicillin-resistant *Staphylococcus aureus* infection in a New Zealand hospital. *N Z Med J* 1987;100:369-73.

- 37 Kac G, Buu-Hoi A, Herisson E, Biancardini P, Debure C. Methicillin-resistant *Staphylococcus aureus*. Nosocomial acquisition and carrier state in a wound care center. *Arch Dermatol* 2000;136:735-9.
- 38 Landman D, Chockalingam M, Quale JM. Reduction in the incidence of methicillin-resistant *Staphylococcus aureus* and ceftazidime-resistant *Klebsiella pneumoniae* following changes in a hospital antibiotic formulary. *Clin Infect Dis* 1999;28:1062-6.
- 39 Law MR, Gill ON, Turner A. Methicillin-resistant *Staphylococcus aureus*: associated morbidity and effectiveness of control measures. *Epidemiol Infect* 1988;101:301-9.
- 40 Linnemann CC, Jr, Mason M, Moore P, Korfhagen TR, Staneck JL. Methicillin-resistant *Staphylococcus aureus*: experience in a general hospital over four years. *Am J Epidemiol* 1982;115:941-50.
- 41 Lugeon C, Blanc DS, Wenger A, Francioli P. Molecular epidemiology of methicillin-resistant *Staphylococcus aureus* at a low-incidence hospital over a 4-year period. *Infect Control Hospital Epidemiol* 1995;16:260-7.
- 42 Mayall B, Martin R, Keenan AM, Irving L, Leeson P, Lamb K. 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;32:257-26.
- 43 Murray-Leisure KA, Geib S, Graceley D, Rubin-Slutsky AB, Saxena N, Muller HA, et al. Control of epidemic methicillin-resistant *Staphylococcus aureus*. *Infect Control Hosp Epidemiol* 1990;11:343-50.
- 44 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 by objectives. *Infect Control* 1987;8:284-8.
- 45 Oto MA, Pinto CME, Martinez CV, Fabio BC, Soza MA, Jerez RA, et al. Control of methicillin resistant *Staphylococcus aureus* at a neonatal ward. *Rev Chil Pediatr* 1992;63:134-8.
- 46 Papia G, Louie M, Tralla A, Johnson C, Collins V, Simor AE. Screening high-risk patients for methicillin-resistant *Staphylococcus aureus* on admission to the hospital: is it cost effective? *Infect Control Hosp Epidemiol* 1999;20:473-7.
- 47 Pearman JW, Christiansen KJ, Annear DI, Goodwin CS, Metcalf C, Donovan FP, et al. Control of methicillin-resistant *Staphylococcus aureus* (MRSA) in an Australian metropolitan teaching hospital complex. *Med J Austr* 1985;142:103-8.
- 48 Pfaller MA, Wakefield DS, Hollis R, Frederickson M, Evans E, Massanari RM. The clinical microbiology laboratory as an aid in infection control. The application of molecular techniques in epidemiologic studies of methicillin-resistant *Staphylococcus aureus*. *Diagn Microbiol Infect Dis* 1991;14:209-17.
- 49 Ribner BS, Landry MN, Gholson GL. Strict versus modified isolation for prevention of nosocomial transmission of methicillin-resistant *Staphylococcus aureus*. *Infect Control* 1986;7:317-20.
- 50 Schlunzen L, Lund B, Schouenborg P, Skov RL. [Outbreak of methicillin resistant *Staphylococcus aureus* in a central hospital]. *Ugeskrift for Laeger* 1997;159:431-5.
- 51 Selkon JB, Stokes ER, Ingham HR. The role of an isolation unit in the control of hospital infection with methicillin-resistant staphylococci. *J Hosp Infect* 1980;1:41-6.
- 52 Shanson DC, Kensit JC, Duke R. Outbreak of hospital infection with a strain of *Staphylococcus aureus* resistant to gentamicin and methicillin. *Lancet* 1976;2:1347-8.
- 53 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.
- 54 Souweine B, Traore O, Aublet-Cuvellier B, Bret L, Sirot J, Laveran H, et al. Role of infection control measures in limiting morbidity associated with multi-resistant organisms in critically ill patients. *J Hosp Infect* 2000;45:107-16.
- 55 Stone SP, Beric V, Quick A, Balestrini AA, Kibbler CC. The effect of an enhanced infection-control policy on the incidence of *Clostridium difficile* infection and methicillin-resistant *Staphylococcus aureus* colonization in acute elderly medical patients. *Age Ageing* 1998;27:561-8.
- 56 Talon D, Rouget C, Cailleaux V, Bailly P, Thouverez M, Barale F, et al. Nasal carriage of *Staphylococcus aureus* and cross-contamination in a surgical intensive care unit: Efficacy of mupirocin ointment. *J Hosp Infect* 1995;30:39-49.
- 57 Tambic A, Power EG, Tambic T, Snur I, French GL. Epidemiological analysis of methicillin-resistant *Staphylococcus aureus* in a Zagreb Trauma Hospital using a randomly amplified polymorphic DNA-typing method. *Eur J Clin Microbiol Infect Dis* 1999;18:335-40.
- 58 Ward TT, Winn RE, Hartstein AI, Sewell DL. Observations relating to an inter-hospital outbreak of methicillin-resistant *Staphylococcus aureus*: role of antimicrobial therapy in infection control. *Infect Control* 1981;2:453-9.
- 59 Yano M, Doki Y, Inoue M, Tsujinaka T, Shiozaki H, Monden M. Preoperative intranasal mupirocin ointment significantly reduces postoperative infection with *Staphylococcus aureus* in patients undergoing upper gastrointestinal surgery. *Surg Today* 2000;30:16-21.
- 60 Yoshida J, Kuroki S, Akazawa K, Chijiwa K, Takemori K, Torisu M, et al. The order of ward rounds influences nosocomial infection. A 2-year study in gastroenterologic surgery patients. *J Gastroenterol* 1995;30:718-24.
- 61 Cooper BS, Medley GF, Stone SP, Kibbler CC, Cookson BD, Roberts JA, et al. Methicillin-resistant *Staphylococcus aureus* in hospitals and the community: stealth dynamics and control catastrophes. *Proc Natl Acad Sci* 2004;101:10223-8.
- 62 Boyce JM. Nosocomial staphylococcal infections. *Ann Intern Med* 1981;95:241-2.
- 63 Mulligan ME, Murray-Leisure KA, Ribner BS, Standiford HC, John JF, Korvick JA, et al. Methicillin-resistant *Staphylococcus aureus*: a consensus review of the microbiology, pathogenesis, and epidemiology with implications for prevention and management. *Am J Med* 1993;94:313-28.
- 64 Spicer WJ. Three strategies in the control of staphylococci including methicillin-resistant *Staphylococcus aureus*. *J Hosp Infect* 1984;5(suppl A):45-9.
- 65 Bell SM. Recommendations for control of the spread of methicillin resistant *Staphylococcus aureus* infection. *Med J Austr* 1982;2:472-4.
- 66 Farr BM, Salgado CD, Karchmer TB, Sheretz RJ. Can antibiotic resistant nosocomial infections be controlled? *Lancet Infect Dis* 2001;1:38-45.
- 67 Crowcroft NS, Catchpole M. Mortality from methicillin resistant *Staphylococcus aureus* in England and Wales: analysis of death certificates. *BMJ* 2002;325:1390-1.
- 68 Centers for Disease Control and Prevention. *Staphylococcus aureus* resistant to vancomycin—United States, 2002. *Morb Mortal Wkly Rep MMWR* 2002;51:565-7.

(Accepted 14 June 2004)

Commentary: Golden rules

Geoff Watts

28 New End
Square, London
NW3 1LS
Geoff Watts
science editor, *BMJ*
geoff@
scileg.freereserve.co.uk

Few events in biology offer a more powerful demonstration of the wonders of natural selection than the spread of antibiotic resistance. Hospital staff struggling to contain the golden staph may, of course, take a more jaundiced view of its triumph.

Fortunately the microbe is not invincible. This week's review by Cooper and colleagues is a reminder that strict isolation measures can limit the spread of methicillin resistant *Staphylococcus aureus* (MRSA).¹ In a similar vein we have the recent report of a successful attempt at eradicating the organism by "ring fencing" elective orthopaedic beds.² The consequent drop in the incidence of postoperative infection allowed surgeons to do more joint replacements. Better research is urgently needed.

The literature on infection control began with Ignaz Semmelweis, a Hungarian physician, in the mid 19th century, and is now extensive. A review by Muto et al on behalf of the Society for Healthcare Epidemiology of America provides a useful insight into our cur-

rent understanding of the spread of MRSA, and so what needs to be done to combat it.³ The key to interrupting transmission is, of course, a firm understanding of what makes it possible. Do dirty rooms, dirty equipment, or dirty habits make the greatest contribution?

As many studies of MRSA have testified, hands (gloved or otherwise) are still the leading culprit. And transmission does not have to be direct. One investigation showed that almost half of the gloves worn by a group of nurses became contaminated with MRSA when they touched not the patients themselves, but various surfaces in the rooms where those patients were being nursed. Another study found the microbe on the keyboards of computers used only by clinicians.

There's evidence too of MRSA from gowns, white coats, all manner of portable equipment from stethoscopes to pagers, domestic items such as mops and furniture, and many types of environmental surface. In one hospital more than a quarter of 350