INFORMATION

METHICILLIN-RESISTANT *STAPHYLOCOCCUS AUREUS* (MRSA)

CYSTIC FIBROSIS TRUST

Report of the UK Cystic Fibrosis Trust Infection Control Working Group

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The UK Cystic Fibrosis Trust Infection Control Working Group

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CONTENTS

For antibiotic treatment of patients chronically infected with MRSA please refer to the Cystic Fibrosis Trust Consensus Document *Antibiotic Treatment for Cystic Fibrosis.*

Grading scheme for recommendations used in Methicillin-resistant *Staphylococcus aureus* (MRSA)

The criteria for the grading of recommendations in this document are based upon a paper by Petrie et al published on behalf of the Scottish Intercollegiate Guidelines Network.

Much of the data in the document are derived from observational studies where randomisation is not appropriate or possible but many are from peer reviewed scientific studies therefore this grading is not always appropriate.

Levels of evidence

Level	*Type of evidence (based on AHCPR, 1992)*
Ia	Evidence obtained from meta-analysis of randomised controlled trials.
Ib	Evidence obtained from at least one randomised controlled trial.
IIa	Evidence obtained from at least one well designed controlled study without randomisation.
IIb	Evidence for at least one other type of quasi-experimental study.
III	Evidence obtained from well-designed non-experimental descriptive studies, such as comparative studies, correlation studies and case control studies.
IV	Evidence obtained from expert committee reports or opinions and/or clinical experience of respected authorities.

Grading of recommendations

Grade	*Type of recommendation (based on AHCPR, 1992)*
A (levels Ia, Ib)	Requires at least one randomised controlled trial as part of the body of literature of overall good quality and consistency addressing the specific recommendation.
B (levels IIa, IIb, III)	Requires availability of well conducted clinical studies but no randomised clinical trials on the topic of the recommendation.
C (level IV)	Requires evidence from expert committee reports or opinions and/or clinical experience of respected authorities. Indicates absence of directly applicable studies of good quality.

Petrie GJ, Barnwell E, Grimshaw J, on behalf of the Scottish Intercollegiate Guidelines Network. Clinical guidelines: criteria for appraisal for national use. Edinburgh: Royal College of Physicians, 1995.

Agency for Health Care Policy and Research. Acute pain management, operative or medical procedures and trauma 92-0032. Clinical practice guidelines. Rockville, Maryland, USA: Agency for Healthcare Policy and Research Publications, 1992.

SUMMARY OF MAIN RECOMMENDATIONS

- All Specialist CF Centres and CF Clinics should have a local infection control policy that addresses MRSA and considers issues of surveillance, hygiene and segregation.
- All Specialist CF Centres and CF Clinics should provide guidance on the importance of hygiene to people with CF, their carers and all staff involved in their care.
- All Specialist CF Centres and CF Clinics should undertake surveillance to ensure that evidence of cross-infection is rapidly detected and appropriate measures put in place to limit spread.

1. INTRODUCTION

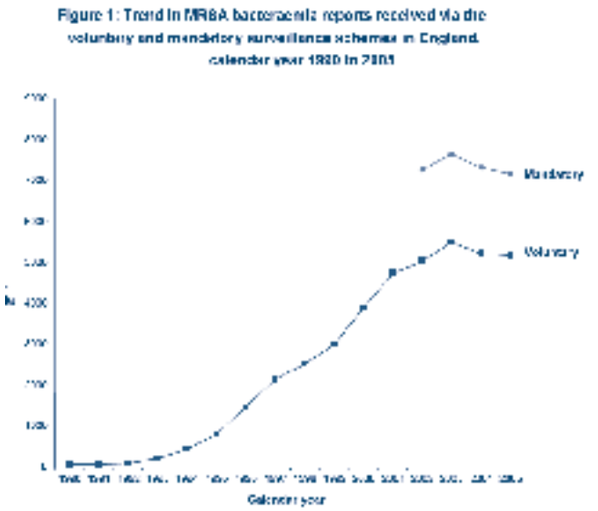
1.1 What is 'MRSA'?

'MRSA' is short for methicillin-resistant *Staphylococcus aureus. S. aureus* is a Gram-positive bacterium. The name 'Staphylo' is derived from ancient Greek, meaning 'bunch of grapes', reflecting the appearance of the organism under the microscope. Methicillin (sometimes referred to as meticillin) was an antibiotic used to treat *S. aureus* in the early 1960s before it was replaced by less toxic alternatives such as flucloxacillin. MRSA is therefore resistant to flucloxacillin, the most commonly used antibiotic for anti-staphylococcal prophylaxis and treatment of *S. aureus* in patients with cystic fibrosis (CF). It is also resistant to other penicillins, cephalosporins and other beta-lactam antibiotics, such as meropenem, imipenem and aztreonam. This resistance is not mediated by the production of enzymes, such as beta-lactamases, but by the production of altered penicillin binding proteins (PBPs) with reduced affinity for flucloxacillin. Hence PBP-2, found in flucloxacillin-susceptible strains, is replaced by PBP-2a and this change is conferred in strains of *S. aureus* which possess the *mec*A gene. Many strains of MRSA in the United Kingdom and Ireland are also resistant to other commonly used antibiotics such as erythromycin and the quinolones e.g. ciprofloxacin.

1.2 Historical aspects

The first reported isolation of MRSA occurred in London in 1961 (Jevons et al, 1961[III]), shortly after methicillin was introduced into clinical practice, and the name 'MRSA' has stuck since then. For many years its clinical significance was questioned until a large increase in isolations and invasive infections affecting most hospitals was reported during the early 1990s (see figure 1) (HPA 2006[III]). In some hospitals in the UK almost half of *S. aureus* bacteraemias are now due to MRSA. MRSA colonises and infects a wide range of vulnerable patients including those with cystic fibrosis. The most common hospital units affected are intensive care units, surgical units, and certain medical specialities such as elderly medicine. The reason may relate to a number of factors, including availability of sites for the organism to colonise, for example surgical wounds or intravenous lines, and the selective pressure exerted by use of antibiotics.

There are a number of different strains of MRSA. Some are particularly common and are known to cause outbreaks in the hospital settings. These are referred to as Epidemic MRSA or EMRSA for short. For reasons that are not absolutely clear, two strains, called EMRSA-15 and EMRSA-16, have been particularly successful in the UK and are now reported from the majority of hospitals. It is likely that most UK Specialist CF centres and CF Clinics will have seen patients colonised or infected with both EMRSA-15 and/or EMRSA-16.



1.3 Community-acquired MRSA

Community-acquired MRSA (CA-MRSA) is defined as any MRSA that has been acquired by a person that has had no contact with hospitals and has no other healthcare-associated risk factors, e.g. receiving care in a residential home. However, this could mean that the strain of MRSA is actually a hospital strain like EMRSA-15 that has been spread between people meeting in the community, only one of whom has been recently hospitalised. Therefore molecular definitions are more reliable to confirm its origin. The *mec*A gene is carried on a mobile genetic element called the Staphylococcal Cassette Chromosome (SCC) *mec*, which is in itself integrated into the chromosome of *S. aureus*. If the strain is SCC *mec* type IV or V and is genetically unrelated to known hospital strains of MRSA it is classified as CA-MRSA (Kluytmans-VandenBergh and Kluytmans, 2006 [IV]).

It is known that there are strains of CA-MRSA that circulate mainly outside of hospitals and are capable of causing infections in previously fit and well individuals. At present they are relatively uncommon in the UK and Ireland but they have become widespread in some parts of the world, particularly in North America and Japan. They are spread by close physical contact and many outbreaks have been described involving nurseries, prisons and sports teams. They usually cause skin and soft tissue infections like boils and impetigo, but can occasionally cause more serious infections that require treatment in hospital, such as pneumonia. These more invasive infections may be caused by CA-MRSA strains that possess the Panton-Valentin leukocidin (PVL) gene. PVL confers greater virulence by encoding for production of cytotoxins which facilitate tissue necrosis and leucocyte destruction (Kluytmans-VandenBergh and Kluytmans, 2006 [IV]). At present there is no published evidence that these strains have caused significant infections in people with CF in the UK and Ireland.

2. CLINICAL CONSEQUENCES OF MRSA INFECTION FOR PEOPLE WITH CYSTIC FIBROSIS

2.1 Lower respiratory tract infection with MRSA in people with CF

Some reports suggest that MRSA does not appear to adversely affect the clinical course for children or adults with cystic fibrosis.

- *A retrospective study of 17 adult patients with MRSA infection at the Royal Brompton Hospital did not identify any significant adverse clinical outcomes associated with MRSA infection (Thomas et al, 1998 [III]).*
- *The overall clinical status, including pulmonary function, nutrition, and chest radiograph appearances did not appear to be adversely affected by MRSA infection among 12 children at the Liverpool Paediatric CF Centre (Solis et al, 2003 [III]).*
- *Two patients at the John Hopkins CF Centre were found to have infection with PVL+ve MRSA strains; however, there was no suggestion of a more virulent course than those patients infected by PVL-ve MRSA strains (Boyle et al, 2005 [III]).*

In contrast several studies support the clinical significance of MRSA in people with cystic fibrosis.

- *At the Leeds CF Centre, children with MRSA in respiratory cultures during a seven year period were identified and compared with controls matched for age, sex, and respiratory function. From a clinic population of 300, ten children had positive sputum or cough swab cultures for MRSA. Children with MRSA showed significant worsening of height standard deviation scores and required twice as many courses of intravenous antibiotics as controls after one year. They had significantly worse chest X-ray scores at the time of the first MRSA isolate and one year later, but showed no increase in the rate of decline in chest X-ray appearance. There was a trend towards lower FEV1 and FEF(25-75) in children with MRSA. There was no significant difference between the two groups with respect to change in weight, body mass index, or Shwachman score (Miall et al, 2001 [IIb]).*
- *A retrospective study at the Washington Paediatric CF Centre found that MRSA had been isolated from 40 of 228 patients between 2001–2004. MRSA isolates from six patients were Panton-Valentin leukocidin (PVL)+ve community acquired strains. Patients who acquired a PVL+ve organism were more likely to be admitted for IV antibiotics, had a higher rate of associated focal pulmonary infiltrates on chest radiographs (including cavitating lung lesions in two cases), higher white cell counts and a greater decline in FEV1 (Elizur et al, 2007 [III]).*
- *A one-year observational study of MRSA in North American CF patients using data from the Epidemiological Study of Cystic Fibrosis demonstrated an association between sputum culture of MRSA and the likelihood of hospitalisation and need for antibiotic treatment (Ren et al, 2007 [III]).*

2.2 Implantable intravenous access devices and gastrostomies

There are potential risks of bacteraemia associated with MRSA infection at intravenous access sites, and peristomal infection complicating gastostomy feeding tubes. Most of the literature relating to placement of intravenous access devices and gastrostomies in non-CF patient populations suggests introducing a program of pre-operative screening and antibiotic prophylaxis.

2.3 Transplantation

Infection or colonisation with MRSA is not considered an absolute contra-indication for solid organ transplantation (Orens et al, 2006 [IV]). Guidelines vary between transplant centres and usually advocate pre-operative screening for MRSA and efforts to eliminate or suppress colonisation or infection with MRSA before transplant surgery.

2.4 Recommendations

- *MRSA infection will lead to a reduction in options for antibiotic treatment and a likelihood of deterioration in lung function, therefore MRSA infection should be avoided [B].*
- *Specialist CF Centres and CF Clinics should follow the local infection control policies for screening and management of MRSA for patients listed for insertion of intravenous access devices and gastrostomies [C].*
- *Specialist CF Centres and CF Clinics should be aware of the policies of the transplant centres for managing patients with MRSA pre and post-transplant [C].*
- *There should be regular communication between Specialist CF Centres and CF Clinics with transplant centres of the infection status of patients under assessment, on a waiting list for transplantation or post-transplantation [C].*

3. PREVALENCE OF MRSA RESPIRATORY TRACT INFECTION IN PEOPLE WITH CYSTIC FIBROSIS

The overall prevalence of lower respiratory tract infection with MRSA among people with CF seems to be increasing. The rate of carriage at non-respiratory sites is unclear. The prevalence of lower respiratory tract infection with MRSA differs between Specialist CF Centres, possibly reflecting regional differences in prevalence of MRSA strains in local healthcare and community settings. The reported prevalence may also be affected by differences in screening policies, infection control practices and use of eradication treatment between Specialist CF Centres.

- *The prevalence of MRSA infection at the Royal Brompton Adult CF Centre increased from 0% in 1980 to 1.7% in 1996 (Thomas et al, 1998 [III]).*
- *At the Leeds Paediatric CF Centre, the prevalence of MRSA infection rose steadily from 0 cases in 1992–1994 to seven cases in 1998 among a clinic population of 300 patients (Miall et al, 2001 [III]).*
- *The prevalence of MRSA at the Liverpool Paediatric CF Centre in 2000 was 6.5% (Solis et al, 2003 [III]).*
- *MRSA was present in sputum samples from 11/164 (6.7%) of patients attending the CF Centre in Florence between 1998–2000. The patients were infected by genotypically different strains (Campana et al, 2004 [III]).*
- *MRSA was present in 11 of 213 (5.2%) sputum samples from 145 patients attending German CF Centres during a six-month period in 2000 (Steinkamp et al, 2005 [III]).*
- *The prevalence of MRSA in US CF Centres has increased from 4.2% in 1999, to 11.8% in 2003 and 14.6% in 2004 (Cystic Fibrosis Foundation Data Registry 2005 [III]).*

3.1 Recommendations

- *The Specialist CF Centre / CF Clinic and local infection control team should be aware of the incidence and prevalence of MRSA at the Specialist CF Centre and in the hospital [C].*
- *Each Specialist CF Centre and CF Clinic should have their own local infection control policy for MRSA [C].*

4. RISK FACTORS FOR ACQUISITION OF MRSA INFECTION

4.1. Studies analysing risk factors for acquisition of MRSA for people with CF

There are very few studies specifically analysing risk factors for acquisition of MRSA for people with cystic fibrosis. In particular, contact with a healthcare facility where MRSA is endemic, and careers in healthcare, seem to be risk factors for acquisition of MRSA by people with cystic fibrosis.

- A study at the CF centre in Sydney between 1993 and 1995 identified seven patients with MRSA infection. Strain typing indicated that transmission of MRSA from the general hospital population was the most likely route of acquisition (Givney et al, 1997 [III]).
- A retrospective case-control study from Leeds was conducted in adults and children with CF, 15 of whom had MRSA-positive respiratory cultures and 30 who were age-sex-matched MRSA-negative controls. During the year prior to initial isolation of the organism, those positive for MRSA spent more time in hospital (mean 19.8 days versus 5.5 days, $p = 0.0003$), received more treatment days of oral ciprofloxacin (mean 43.5 days versus 13.9 days, $p = 0.03$), more treatment days of oral/intravenous cephalosporins (mean 42.7 days versus 15.4 days ($p = 0.04$), and were more likely to be colonised/infected with *Aspergillus fumigatus* (40% versus 10%, $p = 0.04$) than the age-sex-matched MRSA-negative controls. Although the strongest association was with admission to hospital, there was no significant difference in observed clinical parameters (clinical and X-ray scores) between the two groups (Nadesalingam et al, 2005 [III]).
- Six of 18 MRSA isolates from patients at the John Hopkins CF Centre had typing patterns consistent with community-acquired strains. Of the 12 patients infected with strains with typing patterns consistent with a healthcare origin, four had careers in a healthcare field involving significant exposure to MRSA (Boyle et al, 2005 [III]).
- A healthcare worker with CF and MRSA infection was treated with eradication therapy but later reacquired a different strain of MRSA. The authors believed the second episode represented a case of transmission as a result of her occupation (Downey et al, 2005 [III]).
- At the Adult CF Centre in Brisbane, genotyping of MRSA isolates from 21 patients revealed that 11 patients were infected by locally endemic strains. The remainder had unrelated strains but several typing patterns resembled those of other MRSA seen in the region. The authors concluded that the results of their study suggested that acquisition of MRSA may be more commonly related to contact with a healthcare facility where MRSA is endemic than person-to-person spread among people with CF (Kidd et al, 2006 [III]).

4.2 Studies analysing risk factors for acquisition of MRSA for people without CF

Other studies conducted in persons without CF have revealed similar associations. The impact of segregation on transmission of MRSA in hospital settings is unclear. Current guidelines for controlling MRSA still recommend isolating patients known to be MRSA-positive during admission to hospital if facilities are available (Coia et al, 2006 [IV]).

- *A case-control study of 67 patients acquiring MRSA during hospital admission found that factors significantly associated with acquisition were receipt of fluoroquinolones (OR 12.1, p = 0.025), receipt of 'intensive care' (OR 8.7, p = 0.002), and an increased number of inter-ward transfers (OR 2, p = 0.019) (Dziekan et al, 2000 [III]).*

- *Another case-control study compared 121 patients infected with MRSA with 123 patients infected with methicillin-susceptible S. aureus (MSSA). Factors significantly associated with MRSA infection were previous use of levofloxacin (odds ratio [OR] 8.01), enteral feeding (OR 2.55) and previous hospitalization (OR 1.95). No association with prior use of penicillins, such as flucloxacillin, was demonstrated (Graffunder et al, 2002 [III]).*

- *Another study evaluated the impact of isolating patients colonized or infected with MRSA on intensive care units and found it had no impact on transmission rates. Strict adherence to hand hygiene was thought to be of greater importance (Cepeda et al, 2005 [IIa]).*

- *A retrospective comparison of care for patients colonised and infected with either MRSA or MSSA showed that the factors associated with an increased risk of MRSA included hospital stay >15 days (adjusted hazard ratio [AHR] 3.22, p<0.001) and previous receipt of fluoroquinolones (AHR 2.57, p<0.001). Prior receipt of ciprofloxacin (AHR 2.53) appeared to confer a higher risk than levofloxacin (AHR 1.77). No other antibiotic classes were significantly associated with an increased risk of MRSA. Interestingly the receipt of narrow spectrum penicillins, including cloxacillin (an antibiotic very similar to flucloxacillin), conferred a protective effect, with patients less likely to acquire MRSA (AHR 0.45) (LeBlanc et al, 2006 [III]).*

- *One study in people without CF demonstrated a significant correlation between failure to isolate patients positive for MRSA and incidence of MRSA on particular hospital wards (Wigglesworth et al, 2006 [III]).*

4.3 Recommendations

- *Admission to hospital is a risk factor for acquiring MRSA and should be balanced against the clinical benefits of inpatient care [B].*

- *Minimise the use of quinolones. Use as targeted therapy for specific infections e.g. against P. aeruginosa in defined early eradication protocols. Avoid empirical use in those not known to be positive for P. aeruginosa [B].*

- *If MRSA-positive patients require admission to hospital, ensure adherence to local infection control policy [C].*

- *People with CF considering careers in healthcare should be made aware of a possible increase in risk of acquisition of MRSA [B].*

5. SCREENING OF PATIENTS WITH CYSTIC FIBROSIS FOR MRSA

Screening for MRSA is an important part of infection control practice in healthcare settings. The most common non-respiratory carriage sites are the nose, axilla (armpit) and groin. Swabs may be tested by direct plating on MRSA-selective agar or more sensitively by enrichment in a selective broth prior to plating on the selective agar. A new PCR test for nose samples is currently under evaluation but the availability of this technology may be limited.

5.1 Recommendations

- *Sputum or cough swabs from people with CF should be sent for microbiological analysis at each hospital visit and be processed using a method that will reliably isolate S. aureus and identify methicillin resistance [C].*
- *Screening of non-respiratory sites should be determined by local infection control policy [C].*
- *In some circumstances such as for elective surgery (e.g. orthopaedic, vascular, cardiothoracic, etc) it may be desirable to screen CF patients for carriage of MRSA at non-respiratory sites, in order to identify those 'at risk' of developing serious infections arising from a carriage site. Screening should be performed either before or on admission to hospital with a view to implementing a decolonisation programme [C].*
- *MRSA positive patients should be isolated according to local infection control policies for the Specialist CF Centre / CF Clinic, and decolonisation/eradication treatment should be considered [C].*
- *If CF Centres or Clinics appear to have a particular problem with MRSA cross- infection, advice from the local infection control team should be sought. Isolates may be referred to the Health Protection Agency for strain typing on a case by case basis [C].*

For comprehensive guidelines for screening for MRSA, visit: www.dh.gov.uk/reducingmrsa

6. DECOLONISATION AND ERADICATION THERAPIES FOR MRSA IN PEOPLE WITH CYSTIC FIBROSIS

6.1 Decolonisation of non-respiratory sites

The aims of decolonisation are to reduce the risk of self-infection with the patient's MRSA and to prevent transmission of MRSA to other patients. Current UK MRSA guidelines outline a number of strategies for decolonisation (Coia et al, 2006 [IV]).

- *Mupirocin-containing nasal ointment (three times a day for five days).*
- *Antibacterial (chlorhexidine, povidine iodine or triclosan) shampoo and body wash (daily for five days). Specialist advice from dermatologists and infection control teams should be taken for patients with chronic skin disorders or neonates.*
- *Systemic antibiotics may be considered to clear persistent carriage in some individuals.*

6.2 Eradication of lower respiratory tract infection

There are a small number of studies of the use of treatment regimens to eradicate MRSA lower respiratory tract infection in people with cystic fibrosis. The rate of clearance of infection without treatment is unknown. The eradication regimens in these studies have included combinations of oral, intravenous and nebulised antibiotics. The optimum regimen remains unclear.

- *At the Liverpool Paediatric CF Centre, an eradication protocol that included the use of topical and nebulised vancomycin was successful in ten of 18 cases. Other measures used included surveillance, strict observation of basic hygienic measures, limiting the use of flucloxacillin, and the removal of implanted intravenous access devices and gastrostomies (Solis et al, 2003 [III]). It should be noted that significant concerns regarding the promotion of vancomycin-intermediate (VISA) and vancomycin-resistant S. aureus (VRSA) would preclude the prolonged use of aerosolised vancomycin, particularly as this would still be considered the main option for intravenous therapy of significant MRSA infections.*
- *A patient with CF and MRSA infection in Brisbane became culture-negative and remained so for the 18 months of follow-up following a two-week treatment course of linezolid (Serisier et al, 2004 [III]). It should be noted that prolonged and repeated use of linezolid has been associated with the emergence of linezolid-resistant MRSA in people with CF (Gales et al, 2006 [III]).*
- *Seven patients at the Adult CF Centre in Brisbane with MRSA infection were treated with a six-month course of rifampicin and sodium fusidate. All patients were infected with the same strain that was endemic at the hospital. MRSA was no longer cultured from sputa of five of the seven patients during and following the treatment course. There was a reduction in the number of days of intravenous antibiotics per six months with 20.3+/-17.6 on treatment compared with 50.7 before treatment and 33.0 after treatment (p=0.02). There was no change in lung function. Gastrointestinal side effects occurred in three, but led to therapy cessation in only one patient. This patient ceased therapy three months into the antibiotic course. MRSA was not cultured in sputum whilst receiving treatment but recurred three months after ceasing therapy. One patient had an isolate that was resistant to rifampicin and did not clear MRSA (Garske et al, 2004 [III]).*

- *At the Manchester Adult CF Centre, 11 patients who were sputum culture +ve for MRSA received antibiotic therapy to eradicate the infection. A number of different treatment regimens were used. All patients eventually eradicated MRSA. Four cases required repeated treatment, two cases received two courses and two cases three courses of different antibiotic regimens before the infection finally cleared (McSorley et al, 2005 [III]).*

- *Successful decolonisation was achieved in 16 of 17 cases at the Belfast Paediatric CF Centre. Repeated attempts were necessary in many patients before successful eradication of infection was achieved: eight patients cleared MRSA following a five day course of rifampicin and fusidic acid, four cases cleared the infection following a further five day course of rifampicin and fusidic acid, and another four patients cleared MRSA after a third course of antibiotics (IV teicoplanin) (MacFarlane et al, 2007 [III]).*

6.3 Recommendations

- *The patient should be kept informed of their infection status [C].*

- *Eradication of MRSA should be attempted for positive cases [B].*

- *The optimal eradication regimen is unclear. A number of options are available (see table 1 and studies listed above). Each Specialist CF Centre / CF Clinic should have a local policy for eradication of infection that covers both non-respiratory and respiratory sites [B].*

- *If one treatment regimen fails to eradicate MRSA infection, two further attempts with the same or different regimens may still be successful and should be considered. Consideration should be given to screening close family members for MRSA and treating as appropriate [B].*

- *If subsequent clinical samples become negative for MRSA, the patient should still be regarded as a potential carrier from the date of the first negative screen for a total of at least six months. A minimum of 3x negative screens of respiratory samples is required during this six-month period, with the final negative screen at least six months after the first negative screen [C].*

6.4 Examples of published eradication protocols for MRSA in people with CF

Northern Ireland Paediatric CF Centre (Macfarlane et al, 2007)

1. Hygiene advice is given to patients and their parents / carers at the start of the treatment course and includes advice on:
   – changing bed linen at the start of treatment
   – use of own towel, face cloth and toothbrush
   – replacement of all nebulisation components

STEP 1:
– Topical mucopirocin 2% to anterior nares twice daily for five days
– Sodium fusidate 50 mg/kg/day for five days
– Rifampicin 20–40 mg/kg/day for five days
– Chlorhexidine for washing

2. Respiratory samples and multi-site swabs are repeated for detection of MRSA on completion of treatment step 1 and again at each clinic visit for up to one year after last isolation of MRSA.

If MRSA persists then proceed to step 2

STEP 2: – Repeat above protocol for a further five days

3. Respiratory samples and multi-site swabs are repeated for detection of MRSA on completion of treatment step 2 and again at each clinic visit for up to one year after last isolation of MRSA.

If MRSA persists then proceed to step 3

STEP 3: – Intravenous teicoplanin 10–15 mg/kg/daily 12h x three doses; then
– Intravenous teicoplanin 10–15 mg/kg/daily once daily for nine to 13 days

4. Respiratory samples and multi-site swabs are repeated for detection of MRSA on completion of treatment step 3 and again at each clinic visit for up to one year after last isolation of MRSA.

Liverpool Paediatric CF Centre (Solis et al, 2003)

I. Surveillance samples: to detect carriers of MRSA.
Obtain swabs from nose, throat, and rectum.

II. Oral/topical vancomycin to eradicate carriage.

1. Treatment of MRSA carrier (five days)
   a. Nasal carriage: 2% mupirocin cream four times a day, or 2% vancomycin cream four times a day.
   b. Oropharyngeal carriage: 2% vancomycin paste (0.5g) four times a day, or 2% vancomycin gel (0.5g) four times a day, or 5mg vancomycin lozenges four times a day.
   c. Gastrointestinal carriage: 40 mg/kg/day oral vancomycin suspension in 4 doses.
   d. Skin carriage: 4% chlorhexidine bath/shower, on alternate days.

2. Treatment of colonization / infection (five days)
   a. Tracheostomy: 2% vancomycin cream two times a day; change foreign body.
   b. Lower airways: Nebulised vancomycin 4 mg/kg/dose, four times a day diluted in normal saline. Patient must receive a dose of nebulised salbutamol prior to vancomycin because of the risk of bronchoconstriction.

III. Limiting use of flucloxacillin.

IV. High level of antistaphylococcal hygiene: including handwashing and device policy.

Brisbane Adult CF Unit (Garske et al, 2004)

Six months treatment with rifampicin (600mg/day, or 450mg/day if weight <50kg) and sodium fusidate (250–500mg twice daily)

7. SHOULD LONG TERM ANTIBIOTICS BE DISCONTINUED FOR PATIENTS INFECTED WITH MRSA?

The use of oral anti-staphylococcal prophylaxis in CF is controversial, but there is no evidence that use of such regimens increases acquisition of MRSA even though the most commonly used anti-staphylococcal agents, flucloxacillin or oral cephalosporins have no activity against MRSA (Smyth, 2003 [III]). However there is no rationale for continuing anti-staphylococcal prophylaxis with flucloxacillin or a cephalosporin once a patient becomes MRSA-positive. Eradication regimens targeted against MRSA contain agents that also have activity against MSSA. If MRSA is successfully eradicated there is no reason why conventional anti-staphylococcal prophylaxis cannot be reintroduced according to unit policy.

For those with co-existent chronic infection with both MRSA and *P. aeruginosa* consideration may be given for utilising aerosolized tobramycin (or gentamicin) instead of colistin, provided the infecting strain of MRSA is susceptible.

7.1 Recommendations

- ***If anti-staphylococcal prophylaxis is used, this should be stopped whilst the patient is on a MRSA eradication regimen [C].***
- ***If MRSA eradication therapy is successful anti-staphylococcal prophylaxis can be reintroduced according to unit policy [C].***
- ***There is no evidence to support the use of amended anti-staphylococcal prophylaxis once a person with CF becomes chronically infected with MRSA [C].***

8. RECOMMENDATIONS TO LIMIT SPREAD

Current medical opinion is that patients with CF with MRSA infection should be segregated from each other and all other people with cystic fibrosis.

Regular attendance and follow-up at a Specialist CF Centre has been shown to be beneficial to both children and adults (Mahadeva et al, 1998 [III]). Therefore avoiding clinic attendance because of fear of MRSA infection is likely to be harmful in that it may seriously interfere with medical care, which will far outweigh any potential risk of acquiring MRSA infection.

8.1 Segregation of people with CF according to MRSA status

8.1.1 Recommendations

- *Every Specialist CF Centre and CF Clinic should have a microbiological surveillance and infection control policy that considers cross-infection risk for MRSA [C].*
- *The methods used and extent to which Specialist CF Centres and CF Clinics segregate patients should be determined by local policy [C].*
- *Good hygiene should be practised in all outpatient clinics and inpatient facilities to minimise the risk of transmission of MRSA between patients [B].*
- *Specialist CF Centres and CF Clinics should monitor the rate of new acquisition of MRSA [B].*
- *A policy of segregation that covers both inpatient admissions and outpatient clinics is advised [C].*

8.2 In the outpatient clinic

Good hygienic measures are of great importance in any Specialist CF Centre or CF Clinic. These should form part of the local infection control policy for the clinic, but the following are recommendations for best practice:

8.2.1 General hygienic measures to limit cross-infection

- *Hand washing or disinfection with alcohol rubs before and after contact with each patient is recommended [B].**
- *Gloves do not obviate the need for hand decontamination and should be worn when there is contact with body fluids and handling of contaminated dressings or linen [C].*
- *Patients should cover their mouth and nose when coughing or sneezing [B].**
- *Patients should wash or disinfect their hands before use of a spirometer or other handheld apparatus [C].**
- *Respiratory function tests should be performed in a well-ventilated room away from other patients [B].**
- *Local infection control policies should be established to prevent contamination and cross-infection from clinic equipment. This will depend on the nature of the equipment [C].*
- *Collection of sputum specimens and cough swabs should be obtained in a well-ventilated room away from other patients [B].**

- *Sputum pots should be covered and soiled tissues must be disposed of in the clinical waste bin immediately after use. Sputum should not be expectorated down toilets, sinks, washbasins or in showers [C].**
- *Airway clearance techniques should be carried out in a separate room away from the waiting area [B].*
- *During physiotherapy appropriate hygienic precautions should be taken to prevent contamination of clothing with respiratory secretions, by the use of disposable aprons [B].*
- *Cleaning of surfaces and apparatus between patients should be specified by local infection control policies [C].**
- *All equipment should be cleaned and dried between patients and maintained according to local infection control policies [C].*
- *Consideration should be given to the potential for cross-infection afforded by toys, books, magazines, computers, game consoles and other communal facilities [C].*
- *Patients should be encouraged to bring their own toys and books and not share them with others [C].*

* also applies to inpatient care

8.3 Additional recommendations for inpatients

- *All MRSA-positive people with cystic fibrosis should be managed in line with local infection control policy [C].*
- *All members of medical, paramedical, nursing and other staff who have physical contact with patients and their immediate environment should practice hand washing or appropriate disinfection of hands between dealing with different patients. This includes everyone who comes into contact with the patient [C].*
- *Patients should have well-ventilated single rooms of an adequate size and there should be en-suite facilities in all rooms [C].*
- *Respiratory function tests, exercise tests, nebulisation and airway clearance treatment sessions should be carried out separately either in the physiotherapy department, a treatment room or in the patient's own room with the door closed [C].*
- *Patients should have their own nebuliser compressor system, oxygen therapy delivery devices and airway clearance devices as required. This equipment should not be shared between patients [C].*
- *Eating and drinking utensils and sweets should not be shared between patients [C].*
- *Food should be consumed in the patients' rooms rather than at a communal table [C].*
- *Rooms should be cleaned between patients according to local infection control policies [C].*
- *Grouping of children with CF for hospital schooling arrangements is no longer appropriate [C].*

8.4 Away from the hospital

Casual meetings between people with CF, including brief encounters indoors and outdoors, carry a small risk of infection; this risk is increased the longer and closer the contact.

8.4.1 Recommendations

- *Patients should discuss cross-infection issues with their CF team and be aware of their own microbiological status [C].*
- *All communal CF camps and holidays should be avoided [B].*
- *CF patients working in the healthcare environment should be aware that they are at greater risk of acquiring MRSA [B].*

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