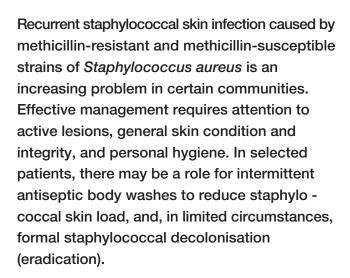
Preventive strategies for recurrent staphylococcal skin infection

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ecurrent staphylococcal infection often commences with the introduction of a new strain of methicillinsusceptible Staphylococcus aureus (MSSA) or, more recently, methicillin-resistant S. aureus (MRSA) into a household or family by an affected individual. Typically, only some household members then develop infection despite likely exposure and even colonisation among other members. This may relate to innate or immune factors, which are currently poorly described, or to a protective effect from carriage of other resident microbial flora.

In an article published in *Medicine Today* earlier this year, Professor Iain Gosbell discussed a range of risk factors for acquisition of community strains of MRSA in particular.1 Prior antibiotic exposure is clearly a major factor, both in the emergence of these strains and in the increase in individual susceptibility to acquisition and disease. The natural history of recurrent staphylococcal disease within a family or household is for recurrences over 18 to 24 months, although some individuals may be affected for much longer even in the absence of overt immunodeficiency.

S. aureus (MSSA and MRSA) is the second most common cause of healthcare-associated bloodstream infections. In recognition of the preventability of most of these events, S. aureus bacteraemia is now a publicly-reported national performance measure for Australian hospitals.2

EPIDEMIOLOGY OF STAPHYLOCOCCAL CARRIAGE

Asymptomatic colonisation with S. aureus is common. As detailed in a recent review,³ cross-sectional studies (point prevalence)

KEY POINTS OF MANAGEMENT: RECURRENT STAPHYLOCOCCAL INFECTION

- Reduce unnecessary antibiotic exposure, including antibiotics for minor or presumably viral infections, to reduce the risk of acquiring community-associated MRSA.
- Avoid entirely the topical use of mupirocin or fusidic acid for impetigo to preserve the susceptibility of MRSA strains to these critically important drugs.
- Treat active skin infections effectively and adopt good personal hygiene when managing infections.
- Maximise skin health and integrity by adopting skin protective behaviours and effective management of pre-existing skin conditions.
- Educate patients about recurrent staphylococcal infection and control measures.
- Use intermittent antiseptic body washes or bathing to break the cycle of recurrence.
- Use formal staphylococcal decolonisation only in situations where recurrent staphylococcal skin disease persists despite the measures described above and the process can be followed in a controlled and organised fashion.
- Also consider decolonisation in selected patients in situations where reducing staphylococcal carriage has proven benefit either to the individual or in the reduction of cross-transmission.
- Always include these five elements in the decolonisation process: i) nasal decolonisation,
 ii) topical body and hair antiseptic wash, iii) consideration of treatment of other householders,
 iv) environmental and personal hygiene measures, and v) follow up to assess control of carriage and disease.

find that about 30% of healthy adults are colonised with the organism. About 20% of the general adult population have persistent or prolonged colonisation with *S. aureus*, roughly 30% have intermittent carriage of the organism, and the remaining 50% seem to be noncarriers. Rates of persistent carriage are higher in children than in adults, with the highest rates seen in neonates (up to 70%). Determinants of carriage are complex and not completely understood.³

The most common site of *S. aureus* carriage is the anterior nares; extranasal carriage can occur in the throat, perineum or gastrointestinal tract. There can also be carriage in cutaneous sites affected by atopic dermatitis or decubitus ulcers, and in catheter exit sites.

Several studies indicate that nasal carriage cannot be demonstrated in many patients colonised or infected with certain strains of community-associated MRSA. In a cross-sectional study of adults and children with S. aureus skin infections and their household contacts, 48% of colonised individuals did not demonstrate nasal colonisation.4 In the largest study of community MRSA colonisation from Sweden, the median duration of colonisation was 5.9 months, with 38% of colonised individuals undergoing some sort of decolonisation or treatment.5 Household contacts with MRSA, young age, carriage of a particular strain (spatype t002) and colonisation in two or more body site locations were significantly associated with a longer duration of colonisation.5 Clinical treatment with antibiotics or MRSA decolonisation were associated with a shorter duration of carriage.5

Persistent carriers have higher loads of *S. aureus*, a higher likelihood of

extranasal carriage sites, and a higher risk of developing S. aureus infection in both community and hospital settings. In a prospective study of hospital-identified MRSA-positive patients, 29% developed infections (28% of which were bacteraemic) over the ensuing 18 months, with 50% manifest after discharge.6 In a US study of patients who had nasal cultures performed at hospital admission, 3.4% were found to be colonised with MRSA and 21% with MSSA.7 A total of 19% of patients with MRSA colonisation at admission and 25% who acquired MRSA colonisation during hospitalisation developed infection with MRSA compared with 1.5% and 2.0% of patients who were colonised with MSSA (p<0.01) and uncolonised (p<0.01), respectively, at admission.7 These findings highlight a role for active decolonisation of MRSA carriers on admission.7

Vitamin D modulates the expression of antimicrobial peptides and cytokine responses in the skin and this may have an impact on infection and colonisation from S. aureus.8 A Norwegian community study found that nonsmoking men aged 44 to 60 years with higher levels of serum 25-hydroxyvitamin D had an odds ratio for MSSA colonisation of 0.44 when compared with men with lower levels (top tertile v. bottom tertile, 95% confidence interval 0.28 to 0.69). No association was demonstrated for women or smokers.9 MRSA was not found in any carriers. An older community study from the USA found that individuals with vitamin D deficiency, who tended to be drawn from more impoverished sections of society, had a statistically significant increased risk of MRSA carriage, but no difference in risk of MSSA.¹⁰ The clinical implications of these studies, performed in two very different populations, are uncertain.

MANAGEMENT APPROACH

An approach to the management of patients with recurrent staphylococcal skin

infection is outlined below. Key points of management are listed in the box on page 66.

PATIENT EVALUATION

The evaluation of a patient with recurrent staphylococcal skin infections begins with a careful history. This should include a history of the infections and their management, the presence and control of underlying skin disorders (e.g. pruritus, dermatitis, dry skin, insect bites) and chronic conditions such as diabetes and renal disease. The existence of recurrent infections of other types that might suggest immune deficiency need to be considered, and risk factors for vitamin D deficiency sought. The patient should also be questioned about whether other house hold members are affected, the size of the household, its location and likely living conditions.

On examination, skin integrity, dryness, ulceration and healed (scarred) areas need to be evaluated. The presence of transcutaneous medical devices, such as an indwelling urinary catheter or a feeding enterostomy, are documented. Particular note should be taken of current active skin disease sites; an example is shown in the Figure. Past microbiological results should be reviewed to confirm what sort of *S. aureus* (MRSA or MSSA) has been cultured.

If a patient has not had infections for three months or more then it is possible that he or she is no longer colonised with S. aureus. Further testing is indicated to clarify the carriage status only if decolonisation is to be considered (see below). Testing by hospitals is often performed to prove 'clearance' of MRSA colonisation so that additional infection control precautions can be suspended. Such testing is usually not performed until more than three months have elapsed since the last positive MRSA culture and involves extensive repeated screening of multiple body sites (nose, throat, perineum, wounds).

There are some very rare primary immunodeficiency states (such as chronic granulomatous disease) that are associated with an increased incidence of staphylococcal disease. Testing for these conditions is indicated only in severe or relapsing cases when control efforts by the measures described below are unsuccessful.

TREATMENT STRATEGIES FOR **ALL PATIENTS**

The management approach to all patients with recurrent staphylococcal skin infection includes treatment of active skin lesions, measures to maximise skin health and integrity, and attention to general hygiene.

Active skin lesions

Active skin lesions should be treated to achieve healing. Principles of management include:

- incision and drainage of boils, if possible
- bathing and application of wound dressings that promote moist wound healing; antiseptics and antimicrobial ointments are not recommended and may delay healing
- for a minority of patients, consideration of systemic antibiotics – for indications, selection and duration, see previous article in Medicine Todav1
- consideration for bacterial skin load reduction strategy as an adjunct to reduce recurrence (see below).

Skin health and integrity

Dry and healing skin should be protected with the following measures:

- use of a sorbalene-based barrier/ moisturiser cream, applied before and after showering
- avoidance of soap exposure nonsoap substitutes should be used when bathing
- avoidance of prolonged exposure to hot water (this removes essential fatty acids from damaged skin, reducing



Figure. A boil on the face in a child.

normal skin function and increasing dryness and pruritus)

- gentle towelling after bathing
- use of active measures to suppress pruritus and techniques to avoid scratching (e.g. short fingernails, wearing of cotton gloves); a trial of oral oil of primrose extract to replace essential fatty acids may assist in pruritus associated with eczema¹¹
- avoidance of shaving of axillae, legs or beard area if infections have occurred in these locations – hair clippers should be used instead or hair removal avoided.

Recurrent staphylococcal infection is a frequent complication of poorly controlled diabetes, peripheral vascular disease, eczematous conditions and other skin diseases. Effective control of these diseases, when present, is important.

General hygiene

Infected skin lesions carry a highly infectious bacterial load. Hands should be cleaned and disinfected before and after touching these lesions and wearing of gloves is advisable. Use of alcohol-based hand rubs is recommended.

Open sores or boils should be covered with clean absorbent dressings and changed regularly as required.¹² Shaving and hair clipping equipment should regularly be cleaned and disinfected.

The environment in households with an affected person has greater environmental contamination of surfaces and fomites with the infecting strain of S. aureus.¹³ Attention to environmental hygiene is worthwhile, especially if decolonisation is attempted because the environmental reservoir may serve as a source for reinfection. General measures include:

- avoiding the sharing of towels, clothing, or other linen that comes in contact with the skin
- washing bed linen regularly (hot wash) and drying it in the sun if possible; airing pillows and mattress
- using tissues rather than a handkerchief, and not nose-picking.

In general, routine use of antiseptic agents in the home is discouraged because it increases selective pressure towards antiseptic resistance.

Treatment strategies for selected patients

Staphylococcal load reduction with topical antiseptics and formal staphylococcal decolonisation are treatment strategies for use in selected patients. The evidence for the role of staphylococcal decolonisation treatment is summarised in the box on this page.3,14-28

Staphylococcal load reduction

Staphylococcal load reduction with topical antiseptics can be used for patients

STAPHYLOCOCCAL DECOLONISATION: RATIONALE AND EFFECTIVENESS

Persistent carriage of S. aureus markedly increases the risk of infection in both healthcare and community settings, and most of these infections are endogenous.3,14 It is reasoned that active decolonisation reduces an individual's risk of subsequent infection due to S. aureus. Furthermore, effective decolonisation of MRSA carriers might also reduce transmission of MRSA in healthcare and other settings.

Results from older, uncontrolled studies have suggested that topical or systemic decolonisation and long-term suppressive therapy were effective for preventing recurrent furunculosis caused by MSSA. However, a Cochrane review published in 2003 of six randomised controlled trials gave no support for either topical or systemic approaches to decolonisation.¹⁵ Four more recent randomised controlled trials assessed the effectiveness of decolonisation for prevention of recurrent staphylococcal skin and soft tissue infections.14 The largest of these trials compared hygiene education only (control group) with three different fiveday regimens: nasal mupirocin alone, or nasal mupirocin given together with either chlorhexidine body washes or dilute bleach (hypochlorite) bath body decontamination.¹⁶ At four months, eradication (decolonisation) was achieved in 48% of participants in the control group, 56% in the mupirocin-only group (p=0.40), 54% in the mupirocin plus chlorhexidine group (p=0.51), and 71% in the mupirocin plus bleach group (p=0.02).16 However, no difference was seen in recurrent skin and soft tissue infection rates.¹⁶ The other three of the four trials were much smaller and relied only on nasal mupirocin as their intervention, with variable results.¹⁷⁻¹⁹ No environmental decolonisation measures were specified in these trials.

The more recent evidence of widespread extranasal colonisation with community MRSA indicates that approaches to decolonisation must include measures to address throat and body surface colonisation. This usually involves use of oral rifampicin, which

must be prescribed with another agent to which the isolate of MRSA is susceptible to avoid emergence of rifampicin resistance (see below).20 Furthermore, it is likely that the household environmental reservoir is significant, 13 and some community strains of MRSA are more transmissible from nonporous fomites.21 Most integrated decolonisation programs include environmental control measures.22-24

Country-wide programs used overseas use active decolonisation of MRSA (in hospitals or the community) to reduce individual risk and/or to reduce risk of transmission of MRSA to other individuals. In the Netherlands, a prospective study of the impact of a two-tiered national decolonisation guideline reported success in 62% with one decolonisation attempt and 80% with a second attempt.22 Treatment in accord with the guideline increased success markedly.²² Some programs target particular 'epidemic' strains of MRSA that are regarded as more able to spread in healthcare settings - Denmark's successful approach to controlling the spread of sequence type 8 MRSA (ST8-UKeMRSA15) is an example of such a program.²³ A similar process is followed in Western Australia.25

Factors associated with failure of decolonisation treatment have been most reliably examined in the Netherlands²⁶ and these have been reviewed.¹⁴ Mupirocin resistance, extranasal MRSA carriage sites (especially the throat) and carriage among household contacts are notable factors.¹⁴ Mupirocin is a critically important agent for decolonisation, and resistance emerges quickly with persistent or prolonged use of the agent;27 this resistance can be avoided by confining mupirocin to intranasal application as part of a dedicated short decolonisation attempt. Fusidic acid is one of the few oral agents available for systemic treatment of established MRSA infection. Significant emergence of resistance has been associated with topical use of this agent, a situation that should have been avoided.28

who have infrequent or minor skin infection recurrences and/or for those patients from home or social situations that are not conducive for formal decolonisation.

Intermittent bathing or showering with triclosan 1%, or aqueous chlorhexidine 4%, or dilute bleach baths (half a cup of bleach in a quarter-filled bath)16,29 can be used to reduce the skin load of S. aureus and thereby reduce the incidence of recurrent infections. This approach is often successful over the long term, without progressing to formal decolonisation. The antiseptic solution should be left in contact with the skin/hair for at least five minutes before being washed off.

Treatment is commenced daily for one week and thence twice-weekly. Once control is gained, treatment can be performed weekly and continued for several months, provided that no skin reactions occur.

Possible problems include:

- failure due to resistance of the staphylococcus to the agent used there are no data on resistance from Australia, but international data indicate that triclosan resistance is common and chlorhexidine resistance is emerging^{30,31}
- drying of the skin from the antiseptic, which then reduces skin integrity and may aggravate infection - this may be prevented by protective skin management together with either a reduction in the frequency of antiseptic use and/or a switch to a different agent
- ingestion or mucous membrane exposure – this should be avoided
- local or systemic allergy to triclosan or chlorhexidine (rare).

Formal staphylococcal decolonisation

In limited circumstances, formal staphylococcal decolonisation (eradication) may be considered. Indications for staphy lococcal decolonisation are listed in the box on this page.^{25,32} Patients with active skin infection should not be decolonised

INDICATIONS FOR FORMAL STAPHYLOCOCCAL DECOLONISATION

Widely accepted indications

- Cooperative patients/households with recurrent staphylococcal skin infection who are able to, and motivated to, follow complex requirements and return for follow up
- Patients colonised with either MSSA or MRSA before cardiac surgery (use preoperative decolonisation or load reduction approach)32
- · Selected hospitalised patients colonised on or during admission with epidemic strains of MRSA or post recovery from major MRSA infection
- Haemodialysis patients colonised with either MSSA or MRSA
- As part of outbreak or endemic MRSA control approach within a facility or institution (requires active screening, isolation, environmental controls, follow up and attention to all potential reservoirs, including staff)

Indications proposed by some or in wide use in some locations

- Patients in the community colonised with epidemic strains of MRSA with proven increased virulence or transmissibility²⁵
- MRSA-colonised patients prior to transfer to residential aged care or rehabilitation facility
- Patients colonised with either MSSA or MRSA prior to major abdominal, vascular, total joint replacement or thoracic surgery32

Situations where decolonisation is not indicated

- Patients with no demonstrable colonisation with either MRSA or MSSA
- Large households, poor prospect of patient co-operation or compliance with treatment measures (use staphylococcal load reduction strategy instead)
- · Patients with active skin infection or dermatitis

as success rates are poor. In addition, decolonisation of individuals with transcutaneous medical devices, chronic respiratory colonisation or chronic skin ulcers should not be attempted in the general practice situation.

Before commencing decolonisation, current staphylococcal carriage status should be determined and the presence of throat colonisation assessed. As a min imum, nose and throat swabs should be collected. The isolate of MSSA or MRSA to be decolonised must be susceptible to mupirocin and any systemic agents prescribed.

Clear instructions are required to gain compliance. Practical patient information is available on the internet from the Australasian Society for Infectious Diseases (see: http://hicsigwiki.asid.net.au/index. php?title=Preoperative_Staphylococcal_ load reduction instruction).33

Other household members are often treated topically at the same time (without initial testing) because crosstransmission is common and other household carriage predicts treatment failure.25 In one study, household decolonisation (i.e. measures taken by all household members regardless of whether they had infections) was shown to be more effective than individual decolonisation in reducing the incidence of subsequent skin and soft tissue infection.34

The initial five-day topical decolonisation protocol involves the following measures. If decolonisation is being attempted for the household then all three parts of the protocol apply to all members:

- nasal mupirocin 2% administered three times daily for five days
- daily antiseptic body wash, including daily hair wash

hygiene measures for the home environment.

Topical antiseptics for body and hair washing are an essential part of the regimen. There are three main options: triclosan 1%, chlorhexidine 4%, and dilute bleach baths. The antiseptic solution should be left in contact with the skin/hair for at least five minutes before being washed off.

In addition to the general hygiene measures described above, measures for the home environment undertaken during a five-day decolonisation treatment may include:

- discarding magazines, newspapers and other clutter
- replacing toothbrushes, razors, deodorant rollers, skin creams and solutions, make-up and make-up brushes
- washing hair brushes, combs, nail files and cutters in the dishwasher (or replacing items)
- wiping daily all frequently touched surfaces in the home, including furnishings, door handles, toilets and taps (large alcohol-containing disposable wipes are simple to use for this purpose)
- on days 2 and 5, cleaning the house well (especially bedrooms and bathrooms) and vacuuming soft furnishings
- on days 2 and 5, hot washing (60°C) clothes, towels, face washers and bed linen

Patients with dentures and patients colonised with some types of MRSA have an increased incidence of throat carriage and require a more intensive approach, either with antiseptic throat gargles (e.g. chlorhexidine 0.1% solution used three times daily) and/or systemic antibiotic treatment with a rifampicin-containing oral combination that penetrates to mucosal level.²⁰ Dentures should be removed each night during the treatment and disinfected (commercial products are available for this purpose).

Domestic dogs and cats may also be

colonised with the same strain of *S. aureus*, but the evidence suggests that this is infrequent.²³ Screening and/or decolonisation of pets is not recommended in most situations.

FOLLOW UP

An organised approach to follow up is essential, utilising community health services and other resources to aid with compliance, treat skin lesions and ulcers and provide patient education. All patients need encouragement to pursue the preventive strategies, especially the measures that aim to improve skin integrity. Patient education should include information about the risks from unnecessary antibiotic exposure.

If triclosan 1% body wash is being used for staphylococcal load reduction and infection recurrence occurs, a change to chlorhexidine 4% or dilute bleach baths can be considered. The patient can be encouraged to adopt the general environmental hygiene measures described above.

If recurrent culture-proven staphylococcal infections continue to occur despite an initial formal decolonisation attempt then possible causes for treatment failure and patient referral to an infectious diseases clinic should be considered. If referral is arranged, use of intermittent antiseptic body washes (see above) can be recommended until the patient's appointment. At clinic review, more prolonged topical and systemic decolonisation attempts (7 to 14 days) with use of oral rifampicin together with a second antibiotic (e.g. oral trimethoprim plus sulfamethoxazole or fusidic acid) for the same period may be attempted.

In the absence of recurrent infections after formal decolonisation, control swabs to assess MRSA clearance are indicated. An exception to this is the setting of a preoperative decolonisation. As a minimum, nose and throat swabs are collected at one, two and three months (refer also to local state and territory protocols – perineum swabs may be required).

In most states, formal MRSA clearance is assessed after more than three months have elapsed since the last positive result and the patient has not received MRSA-specific antibiotics for at least three months. Two clearance control sets of swabs (nose, throat) are collected on the same or different days and tested separately.³⁵

FINAL COMMENTS

S. aureus, a ubiquitous human commensal, remains a formidable or troublesome pathogen in many individuals. Although the management strategies described here are frequently successful, more effective measures will depend on a better understanding of the pathogen and its complex interactions with the human host.

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