Screening for meticillin resistant *Staphylococcus aureus* (MRSA): who, when, and how?

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Meticillin resistant *Staphylococcus aureus* (MRSA) remains one of the foremost nosocomial pathogens. The changing epidemiology and microbiology of MRSA worldwide provides an important context for decision making with regard to infection prevention and control. MRSA can be categorised as hospital associated, community onset, community associated, or livestock associated. This article concentrates on hospital associated MRSA, although both community associated and livestock associated MRSA are important emergent threats.

Patients colonised or infected with MRSA provide a reservoir within hospitals. Transmission occurs directly from patient to patient, indirectly via the hands of hospital staff after contact with a patient who is colonised or infected, or after handling contaminated materials, or by direct patient contact with the contaminated environment.

Infection prevention and control measures minimise risk of transmission to prevent healthcare associated infection. Although there is broad agreement on the control measures required for patients colonised or infected with MRSA, there is considerable controversy over the optimal strategy and extent of screening that should be undertaken.

**Whom should we screen for MRSA?**

One of the most contentious issues is whether all patients should be screened for MRSA on admission to a healthcare facility. Advocates of universal screening assert this strategy self evidently offers the highest probability of detecting MRSA carriage. Others argue that universal screening programmes are costly and that testing should be targeted based on known risk factors for MRSA colonisation. However, a prospective case-control study of more than 12 000 patients showed that screening strategies of sufficient sensitivity require screening of 65% of admissions, and the additional complexity of accurately identifying those at increased risk of MRSA carriage may lead to carriers being missed. Thus, even if identifying populations at high risk for MRSA carriage may be feasible, universal screening may be easier to implement.

In Scotland modelling performed as part of a Health Technology Assessment study indicated that universal screening was potentially both effective and cost effective as part of a strategy to control MRSA. However, a subsequent large prospective study involving almost 70 000 patients showed that screening of all admissions to “high risk” specialties (intensive care, orthopaedics, renal medicine, vascular surgery, and cardiothoracic surgery) combined with targeted screening of all admissions on the basis of a three question clinical risk assessment (see box 1) achieved similar detection rates (50-53%) as universal swabbing but at significantly reduced cost. This strategy has subsequently been implemented throughout Scotland.

However, this clinical risk assessment has been validated only in Scotland, in a setting of high prevalence of hospital associated MRSA, and key risk factors may vary by country. For example, in Denmark animal husbandry and hospitalisation in another country are the main risk factors. Known risk factors for MRSA colonisation among adults in acute care settings have recently been summarised in a systematic review by Xue et al.

**When should we screen for MRSA?**

Elective hospital admissions should be assessed according to local policies to ensure results of the colonisation assessment are available before admission, to facilitate patient management. All other admissions eligible for screening according to local policies, should be screened at the earliest opportunity. This ensures appropriate interventions can be applied as soon as possible to reduce risk of infection in individual patients and prevent transmission to others.

**SUMMARY POINTS**

- Controversy exists over the optimal strategy and extent of screening for meticillin resistant *Staphylococcus aureus* (MRSA)
- Individual clinicians must be aware of, and comply with, local screening and management policies for MRSA colonised patients
- Standard screening swabs should include (a) a nasal swab and a perineal swab or (b) a nasal swab and a throat swab as the minimum
- Screening identifies colonised or infected patients who can then be managed to decrease spread of MRSA, including contact precautions, decolonisation, and isolation
- Screening results need to be available in a timescale that allows effective intervention to reduce risk of infection in individual patients and prevent transmission to others

**METHODS**

We undertook a literature review using search terms from a previous systematic review of MRSA screening and updated to June 2013. We searched Medline and the Cochrane Library using the terms: “MRSA screening”, “infection prevention and control”, “risk factors”, and “decolonisation”. We also drew on our own experience derived from involvement in national guidance development on control of MRSA and implementation of a national MRSA screening programme. Most evidence published to date is observational, and therefore the overall quality of evidence is weak to moderate.

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**Box 1 | Clinical risk assessment questions used to target MRSA screening in Scotland**

1. Has the patient any history of MRSA colonisation or infection at any time?
2. Has the patient been admitted from somewhere other than their own home?
3. Does the patient have a wound or ulcer or indwelling medical device that was present before admission to hospital?
Box 2 | Predictive risk factors for MRSA colonisation among adults in acute care settings

| Hospitalisation within the past 24 months |
| Admission to a long term care facility or a rehabilitation facility within the past 18 months |
| Admission to an intensive care unit in the past 5 years |
| Intra-hospital transfer |
| Surgical intervention within the past 60 months |
| Indwelling urinary catheter |
| Antibiotic use within the past 12 months |
| Presence of skin lesion |
| Previous MRSA colonisation |
| Comorbidity of chronic health evaluation class C or D (that is, patient has severe activity limitation because of chronic disease or is bedridden) |
| Presence of terminal illness |

| Male |

*Adapted from Xue Y et al (2012)*

How should we screen for MRSA?

A large, national, cross sectional study, which screened more than 10,000 patients for MRSA from nose, throat, axilla, perineum, and wound or device sites, found that a nasal swab identified only 66% of MRSA carriers. Addition of a second and further swabs increased the detection rate, with nose and perineum swabs identifying 82% of cases. The axilla was the least useful site for identifying carriers (8% detection rate, see table). Standard screening methods should include two swabs (a nasal swab plus a perineal or throat swab) as the minimum.

What is the duration of MRSA colonisation?

It is not known how long MRSA colonisation persists, or how long after an episode of MRSA infection a patient still tests positive for MRSA. A recent longitudinal study over four years, assessing over 1500 MRSA positive patients, showed that during the first year about half the patients remained MRSA positive. There was a further slow reduction in colonisation during second to fourth years with about 20% of patients remaining positive at the end of the period. This result probably reflects the existence of two groups of patients – those who are transiently colonised and quickly lose MRSA, and those who are chronic carriers, for whom MRSA becomes established as part of their “normal” flora. For practical purposes, patients who previously tested positive for MRSA should be presumptively regarded as still positive and screened appropriately.

| Number of swabs testing positive for MRSA by anatomical site (detected on chromogenic agar) and percentage positive compared with the gold standard | (Adapted from Matheson et al 2012)* |
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| **Anatomical sites** | **No of samples positive for MRSA (n=298)** | **Percentage (95% CI) detection (versus gold standard)** | **Percentage (95% CI) extra detection with extra sites used (versus nasal alone)** |
| Nasal alone | 198 | 66.4 (60.9 to 71.6) | — |
| Axilla alone | 23 | 7.7 (5.2 to 11.3) | — |
| Throat alone | 103 | 34.6 (29.4 to 40.1) | — |
| Perineum alone | 107 | 33.9 (30.7 to 41.5) | — |
| Nasal + axilla | 205 | 68.8 (63.3 to 73.8) | 2.4 (0.95 to 4.8) |
| Nasal + throat | 238 | 76.5 (71.4 to 81.0) | 10.1 (6.9 to 14.1) |
| Nasal + perineum | 245 | 82.2 (77.5 to 86.1) | 15.8 (11.8 to 20.4) |
| Nasal + throat + axilla | 234 | 75.1 (75.3 to 82.8) | 12.1 (8.6 to 16.3) |
| Nasal + throat + perineum | 269 | 90.7 (86.3 to 93.9) | 23.8 (19.1 to 29.1) |
| Nasal + axilla + perineum | 250 | 83.9 (79.3 to 87.6) | 17.5 (13.3 to 22.3) |
| Nasal + throat + axilla + perineum | 273 | 91.6 (87.9 to 94.3) | 25.2 (20.3 to 30.5) |

*Gold standard was all anatomical swab sites combined, pooled in nutrient broth and cultured on chromogenic agar.*

What do we do next?

Screening identifies colonised or infected patients, who can then be managed to reduce the risk of endogenous infection and transmission to other individuals. For elective surgery where antibiotics are indicated, MRSA positive patients should be given an antibiotic that provides cover against MRSA. The main interventions to decrease spread of MRSA are isolation and decolonisation. Isolation protects others, whereas decolonisation primarily prevents infection in the individual. Although the effectiveness of any single infection prevention and control measure in isolation is uncertain, collective use of the standard range of methods against MRSA reduces prevalence. A Cochrane review of the evidence for isolation in control of MRSA colonisation concluded it was difficult to determine the contribution of individual measures when they do not act independently and are often implemented concurrently. Despite this, isolation is advocated as a measure to control cross transmission of MRSA in hospital. The evidence with respect to decolonisation is slightly stronger.

A systematic review of the efficacy and cost effectiveness of screening and interventions to reduce MRSA colonisation describes treatment with mupirocin nasal ointment (three times daily for five days) combined with five days’ use of antisep tic wash. The clearance rate two days after completion of the regimen was 53%. A more recent systematic review had similar findings and highlighted colonisation at non-nasal sites being associated with failure of topical decolonisation. A well designed multicentre randomised controlled trial with 146 chronic carriers of MRSA showed 74% clearance at three months after decolonisation when systemic decolonisation (seven day course of rifampicin and doxycycline) was added to the standard regimen.

Reasons for decolonisation failure include patient compliance with the treatment regimen, so the information given to patients is critical (box 3). A cross sectional survey of home based decolonisation regimens for MRSA colonised patients indicated wide variations in the information given by hospital and community healthcare workers, risking variation in application of the regimen.

Normally a maximum of two decolonisation courses are given as part of a screening programme. If a patient still tests positive after the second course, appropriate advice on infection prevention and control should be offered to the patient (box 3), and advice on subsequent treatment should be sought from a consultant microbiologist. Antimicrobial resistance is of concern with respect to widespread use of any antibiotic as part of decolonisation regimens. A large randomised controlled trial found that substantial increases in resistance to mupirocin can occur after repeated or extended courses of the antibiotic, and, to maximise the potential therapeutic benefits of mupirocin, it is recommended that such use is avoided.

Do we need to check for clearance of MRSA?

The evidence base for rescreening after decolonisation is weak. Rescreening is generally performed weekly for three weeks, starting at least two days after completion of treatment to ensure the burden of colonisation has been reduced before any surgical intervention. Thereafter, rescreening is not advised unless clinically indicated.
Box 3 | Interventions to reduce MRSA colonisation

Decolonisation

A standard decolonisation regimen would involve:

– Application of mupirocin nasal ointment three times daily for five days. If applied properly, the patient should be able to taste the mupirocin.

– Use of an antiseptic wash, usually chlorhexidine, for five days. This should be used undiluted as a liquid soap. Apply it directly to the wet skin using hands or a cloth. It should be left in contact with the skin for at least a minute. About 25 ml of chlorhexidine should be used for each shower or wash, starting at the face and working downwards, paying particular attention to the armpits and groin. Rinse and repeat for a second wash but this time include the hair. This should not be used in conjunction with other soaps or shampoos, which may inactivate the disinfectant.

– Daily changing of bed linen and towels is considered optimal practice, though some patients may find this overly burdensome and difficult to adhere to.

Contact precautions

These are a set of infection control measures designed to prevent transmission of infectious agents spread by direct and indirect contact with patients and healthcare workers. They include isolation (preferably with en suite facilities), hand hygiene, use of personal protective equipment (gloves, gown), equipment care, environmental decontamination, and the safe handling of linen and waste.

as suppression of colonisation is short lived in most of those treated. A small prospective cohort study (n=137) examined the long term efficacy of a standardised decol

37

References


The knowledge that TXA reduces bleeding in surgery and reduces mortality in trauma raises the possibility that it might also be effective in gastrointestinal bleeding. Fibrinolysis may play a role in gastrointestinal bleeding because of premature breakdown of fibrin blood clots at the bleeding site. Many patients with acute upper gastrointestinal bleeding have elevated levels of fibrin degradation products (a marker of fibrinolysis), and these patients have worse outcomes.

**What is the evidence of the uncertainty?**

Through searches of PubMed, Embase, and the Cochrane Central Database of Controlled Trials, we identified nine randomised comparisons from eight clinical trials of the use of TXA in upper gastrointestinal bleeding and none in lower gastrointestinal bleeding (figure). Seven of the identified trials were also included in a Cochrane systematic review on the effectiveness of TXA in upper gastrointestinal bleeding. The pooled result shows a statistically significant reduction in the risk of death in patients receiving TXA (relative risk 0.66, 0.47 to 0.93) (figure). However, the quality of the trials was poor. Only one trial had adequate allocation concealment. In several trials, patients were excluded after randomisation, and information on their outcomes was not reported, raising the possibility of selection bias. All but two trials were conducted before the widespread use of therapeutic endoscopy and proton pump inhibitors. Therefore, their results might not be applicable to current patients with gastrointestinal bleeding.

We conducted a trial sequential analysis to assess the reliability of the result from our systematic review and meta-analysis. This showed that about 5500 patients would need to have been included in clinical trials (many more than the current total) to have enough power to detect a plausible treatment effect. Thus, although the meta-analysis result is statistically significant (P<0.05), this could easily be a false positive result.

Only three trials reported data on adverse events. These studies were already included in the previous Cochrane review. The risk of thromboembolic events is about 1% overall and seemed to be higher in TXA treated patients (relative risk 1.86, 0.66 to 5.24). However, the result is imprecise and compatible with the play of chance.

Given these uncertainties, TXA is not routinely used or recommended for gastrointestinal bleeding. In a UK audit in 2007, fewer than 1% of patients with upper gastrointestinal bleeding received TXA. TXA is not referred to in two international consensus documents on the management of upper gastrointestinal bleeding nor in the 2012 UK National Institute for Health and Care Excellence (NICE) guidelines for acute upper gastrointestinal bleeding.

**Is ongoing research likely to provide relevant evidence?**

Searches of the ClinicalTrials.gov trial registry suggest that there are two ongoing double blind randomised controlled trials of the use of intravenous TXA in gastrointestinal bleeding (described in the table). In both trials, TXA or placebo is given in addition to the usual management of gastrointestinal bleeding.

The TAUGIB trial includes patients with acute upper gastrointestinal bleeding before undergoing endoscopy, but it will not be large enough to determine reliably the effect of TXA on mortality and thromboembolic events. Assuming a mortality of 10% in the placebo group, a trial of 400 patients has only 10% power to detect a 25% reduction in mortality (10% to 7.5%).

The HALT-IT trial aims to recruit 8000 patients with acute gastrointestinal bleeding (upper or lower) and will have over 90% power to detect a 25% reduction from 10% to 7.5% in mortality.

**What should we do in the light of the uncertainty?**

TXA is not routinely recommended for upper or lower gastrointestinal bleeding, and there are important uncertainties about its safety and effectiveness for this indication. Uncertainty about its effect on thromboembolic events is important, as many patients with acute gastrointestinal bleeding are older and have a high baseline risk of thromboembolism. In a UK survey, the median age of patients with gastrointestinal bleeding was 68 years, with about 18% having a history of ischaemic heart disease and 8% with a previous stroke. Clinicians have to decide whether to use TXA without reliable evidence of the balance between risk and benefit. However, in the context of such uncertainty the most appropriate management would be
to include them in a randomised controlled trial. This will ensure that the uncertainty is resolved in a timely and scientifically defensible way.

In the meantime, current NICE guidelines suggest the following key points in the management of patients with upper gastrointestinal bleeding:

- Risk assessment, with Blatchford scoring system at first assessment and the full Rockall scoring system after endoscopy
- Fluid resuscitation
- Localisation of the bleeding site
- Therapeutic interventions to stop bleeding, including endoscopic treatment
- Prevention of re-bleeding.

NICE guidelines are useful for standardising the management of acute upper gastrointestinal bleeding. However, the evidence base for some of the recommendations is weak. In addition, no recent guidelines are available for lower gastrointestinal bleeding. High quality research is needed to inform clinical decisions in the management of both upper and lower gastrointestinal bleeding.

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ANATOMY QUIZ

Lateral radiograph of the right wrist

A: Scaphoid bone
B: Pisiform bone
C: Capitate bone
D: Lunate bone
E: Styloid process of the ulna

CASE REPORT

Weight loss in an adolescent girl

1 This picture is caused by excessive vomiting in patients with an eating disorder who are underweight or normal weight. It can also be seen in patients who have been severely restricting their diet or have stopped eating but have had feeding reinstated, putting them at risk of refeeding syndrome.

2 There are several physical and psychological complications of anorexia nervosa in adolescents, which result in disrupted physical and emotional development.

3 Family based therapy.

4 Measurement of weight and BMI, hydration status, and temperature. Tests of cardiovascular health (pulse; blood pressure, including lying-standing measurements; and electrocardiography) can also be useful.

5 Yes (in England and Wales).