Use of surveillance cultures and enteral vancomycin to control methicillin-resistant \textit{Staphylococcus aureus} in a paediatric intensive care unit

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\textbf{ABSTRACT}

This study assessed the effects of throat and gut surveillance, combined with enteral vancomycin, on gut overgrowth, transmission of methicillin-resistant \textit{Staphylococcus aureus} (MRSA), infections and mortality in patients admitted to a paediatric intensive care unit (PICU). A 4-year prospective observational study was undertaken with 1241 children who required ventilation for \(\geq 4\) days. Patients identified as MRSA carriers following surveillance cultures of throat and rectum received enteral vancomycin. Twenty-nine (2.4\%) children carried MRSA, 19 on admission and nine during treatment in the PICU; one patient was not able to be evaluated. Overgrowth was present in 22 (75\%) of the carriers. Ten (0.8\%) children developed 21 MRSA infections (15 exogenous infections in eight children at a median of 8 days (IQR 3–10.5); five primary endogenous infections at a median of 3 days (IQR 1–25) in three children when they were in overgrowth status; one child developed both types of infection). Enteral vancomycin reduced gut overgrowth significantly, completely preventing secondary endogenous infections. Transmission occurred on nine occasions over a period of 4 years. Four patients died, two (5.9\%) with MRSA infection, giving a mortality (11.8\%) similar to the study population (9.8\%). No emergence of vancomycin-resistant enterococci or \textit{S. aureus} with intermediate susceptibility to vancomycin was detected. A policy based on throat and gut surveillance, combined with enteral vancomycin, for critically-ill children who were MRSA carriers was found to be effective and safe, and challenges the recommended guidelines of nasal swabbing followed by topical mupirocin.

\textbf{Keywords} \ Gut overgrowth, infection control, MRSA, paediatric ICU, surveillance, vancomycin

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\textbf{INTRODUCTION}

Methicillin-resistant \textit{Staphylococcus aureus} (MRSA) was first identified in the UK in the 1960s [1], and was isolated for the first time in the USA in an outbreak in Boston in the late 1960s [2]. Since that time, the incidence of MRSA infections has continued to increase [3,4], and spread of MRSA is now an international problem [5]. The MRSA infection rate in children was believed originally to be lower than in adults. However, recent studies have reported an increasing incidence of bloodstream infections caused by MRSA acquired in the paediatric care setting [6,7]. Neonatal units are another area of concern, with several reported outbreaks of severe MRSA pneumonia and septicaemia [8,9].

Nasal carriage of MRSA has been considered to be the source of invasive MRSA infections, and is thought to be crucial in the spread of MRSA [10]. Topical mupirocin has been recommended widely for the clearance of nasal MRSA [11]. Infection control programmes that include nasal screening, combined with intra-nasal mupirocin, skin decontamination with an antimicrobial soap, and placement of patients under contact isolation precautions, were only effective temporarily in the control of MRSA transmission [12,13]. Indeed, two randomised trials that evaluated nasal mupirocin for clearing MRSA showed poor efficacy in...
eradicating extra-nasal body sites, including the gut [14,15].

Oropharyngeal and gastrointestinal carriage of MRSA in children and adults is an important source of MRSA infection [16,17]. Nasopharyngeal and gut flora determine skin carriage on the upper part of the body, such as the hands, arms and axillae, and the lower part of the body, including the perineum and inguinal areas, respectively [17]. Touching intact areas of the skin during patient care can result in contamination of healthcare workers’ hands with MRSA present on the patient’s skin, and may lead to the transmission of MRSA via the carers’ hands to other patients. A policy based on surveillance cultures of throat and rectum, combined with enteral vancomycin, has been used effectively to control MRSA outbreaks in ventilated adult patients [18–21]. The present study investigated the efficacy of this policy in controlling MRSA in critically-ill children.

PATIENTS AND METHODS

Setting

The study was conducted in a 20-bed regional paediatric intensive care unit (PICU), with an admission rate of >1000 patients/year. Of total admissions, 40% are for post-operative cardiac care, 40% are for medical conditions, and the remainder are for surgical conditions, including burns. Overall mortality in the unit is 4.5%, with a predicted mortality rate of 6.25% calculated with the paediatric index of mortality (PIM) [22], and a standardised mortality rate of 0.72.

Design and endpoints

The primary aim of this prospective observational single-centre study was to determine the efficacy of a strategy using surveillance cultures of throat and rectum, combined with enteral vancomycin, in the eradication of MRSA carriage and the prevention of secondary endogenous MRSA infections. A secondary endpoint was to monitor the emergence of vancomycin-resistant enterococci (VRE) and Staphylococcus aureus with intermediate susceptibility to vancomycin (VISA) [23].

Patients

The study was conducted during a 48-month period between 1 March 1999 and 28 February 2003. The subjects were children admitted to the PICU who required mechanical ventilation for a minimum of 4 days. The institutional ethics review board approved the study.

Antibiotic policy

The criteria used for the choice of an antimicrobial agent for either prophylaxis or treatment, were: (i) protection of the indigenous flora, which is required to control the overgrowth of MRSA. Cephradine was used as the first-line anti-staphylococcal agent, as flucloxacinil disrupts gut ecology to a greater extent than does cephradine [24]; (ii) the use of antimicrobial agents with the lowest potential for the development of resistance, defined as agents to which no resistance has emerged within 2 years of general use. Antimicrobial agents with a high potential for the development of resistance, such as linezolid, were only prescribed on a restricted basis [25]; (iii) the use of agents with anti-inflammatory properties, e.g., aminoglycosides and glycopeptides, or treatment with β-lactams and fluoroquinolones, which may increase cytokine production [26].

Antibiotic use fell into three categories: (i) surgical prophylaxis; (ii) selective decontamination of the digestive tract, i.e., patients with the abnormal carrier state, colonisation or infection (e.g., with aerobic Gram-negative bacilli (AGNB) and/or MRSA) received enteral polymyxin E/tobramycin [27] and/or vancomycin [28] (Table 1); and (iii) therapeutic intravenous regimens.

Device policy

Staphylococci, both coagulase-positive and -negative, have an affinity for plastic devices. Most patients who require long-term intensive care have indwelling devices, including intubation tubes, intravascular lines and urinary catheters, tracheostomy and/or gastrostomy tubes. The chance that these devices become contaminated with MRSA is substantial in a patient who is a carrier of MRSA in the nose, throat, gut or skin [29]. A strict device policy was in place in the PICU. Devices were changed immediately for any case in which diagnostic samples were positive for MRSA; e.g., in the case of positive tracheal aspirates, the ventilation tube was replaced; in the case of a positive blood culture taken through an indwelling vascular line or a positive vascular catheter site swab, the intravascular lines were removed and replaced.

Sampling policy

Surveillance samples of throat and rectum were taken on admission to detect the importation of MRSA, and thereafter twice-weekly (Monday and Thursday) to identify acquisition of MRSA in the PICU. Surveillance samples were distinguished from diagnostic samples, which were taken solely on clinical indication from normally sterile sites, including lower airways, blood and wounds.

Table 1. Enteral and topical vancomycin treatment regimens [28]

<table>
<thead>
<tr>
<th>Carriage site</th>
<th>Enteral treatment for 5 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nasal</td>
<td>2% cream</td>
</tr>
<tr>
<td>Oropharyngeal</td>
<td>2% paste (0.5 g) or 5 mg lozenge</td>
</tr>
<tr>
<td>Gut</td>
<td>40 mg/kg/day oral suspension</td>
</tr>
<tr>
<td>Skin</td>
<td>4% chlorhexidine bath/shower</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Colonisation/infection site</th>
<th>Topical treatment for 3 days and enteral treatment for 5 days (as above)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lower airways</td>
<td>Nebulised 5 mg/kg/day</td>
</tr>
<tr>
<td>Wounds</td>
<td>2% aquafilm or 2% tauroline dressing</td>
</tr>
<tr>
<td>Gastro/tracheostoma</td>
<td>2% paste</td>
</tr>
</tbody>
</table>

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Microbiology

Surveillance samples

Surveillance cultures of throat and rectal swabs were processed qualitatively and semiquantitatively to detect the level of MRSA carriage [30]. Each swab was streaked on to Staphylococcus medium no. 10 (Oxoid, Basingstoke, UK) using the four-quadrant method, and then the tip was broken off into 5 mL brain-heart infusion enrichment broth (BHI; Oxoid). All cultures were incubated at 37°C. The agar plate was examined after incubation for 1 and 2 nights. Additionally, if the enrichment broth was turbid after overnight incubation, it was then inoculated on to a Staphylococcus agar plate. A semiquantitative estimation was made by grading growth density on a scale of 1+ to 5+ [31].

Diagnostic samples

Lower airway secretions, urine and pus were processed in a qualitative and semiquantitative way with standard microbiological methods. Blood cultures were processed using the BACTEC 9240 system (Becton Dickinson, Oxford, UK). S. aureus isolates were tested for methicillin susceptibility by a strip diffusion method (Mast, Bootle, UK) on Mueller-Hinton agar (Oxoid) containing NaCl 2% w/v. Test cultures were inoculated in streaks across the plate, and a strip containing 25 μg methicillin was applied across the streaks. Plates were incubated at 30°C for 24 h. S. aureus isolates growing up to the strip were tentatively classified as methicillin-resistant. Resistance was confirmed by a methicillin MIC of ≥8 mg/L with Etest® (AB Biodisk, Solna, Sweden) [32], and with the Mastalex-MRSA latex agglutination test for PBP2a (Mast). MICs of vancomycin were determined with Etests; S. aureus isolates with MICs of 8–16 mg/L were defined as intermediate-susceptible [33]. Faecal samples and rectal swabs from all patients were screened for enterococci as described by Endtz et al. [34]. Vancomycin MICs were determined by Etest, with enterococci with MICs ≥16 mg/L defined as resistant [35].

Infection control policy

When MRSA was isolated from any site, the patient was moved to an isolation cubicle and cared for as an infected case. Swabs were taken from anterior nares, throat and rectum to determine the extent of carriage. If more than one case occurred, all patients who had been in the same ward during the 3-day period before the index case was identified had swabs taken from anterior nares and throat/rectum. Nursing staff who attended the index case had swabs taken of anterior nares, throat, and rectum, and the occupational health department was informed. If the index case had undergone surgery, children on the same surgical list were screened. If any patients were positive, they were managed in the same way as the index case. If any staff were positive, they were treated as an index case and excluded from work until all screening swabs were negative.

Terminal cleaning of cubicles

All equipment used was cleaned in the cubicle and removed before the cleaning schedule. All horizontal surfaces were cleaned with a solution of detergent and water, followed by disinfection with a solution of a chlorine-releasing agent at a concentration of 10 000 ppm available chlorine (Haz-tab Granules H8800; Guest Medical, Edenbridge, UK) and then dried thoroughly. Any curtains were sent to the laundry. Vertical blinds were cleaned in the same way as surfaces and by vacuum attachment.

Definitions

A patient was defined as a carrier if MRSA was isolated from at least two consecutive surveillance samples of throat and/or rectum, in any concentration, for a period of at least 1 week [36]. Overgrowth was defined as the isolation of MRSA in a concentration graded at least 3+, or ≥10^7 CFU/mL of saliva or/g of faeces [19]. Infection was defined as a microbiologically proven clinical diagnosis of inflammation (local and/or generalised). This included not only clinical signs, but also the presence of a moderate (+ +) number of leukocytes and MRSA (≥3+ or ≥10^7 CFU/mL) in diagnostic samples obtained from an internal organ, or the isolation of MRSA from a blood culture [36]. All infections were diagnosed according to CDC criteria [37]. Primary endogenous infection was defined as infection caused by MRSA that was already carried upon admission to the PICU [20]. This type of infection occurs generally within 1 week of admission to PICU. Secondary endogenous infection was defined as infection caused by MRSA acquired after admission to the ICU, i.e., the initial throat and gut swabs were negative for MRSA, but became positive subsequently. The mechanism of spread of potentially pathogenic microorganisms (PPM), including MRSA, is usually transmission via the hands of carers, with acquisition in the oropharynx, followed by carriage and overgrowth in the digestive tract. Subsequently, colonisation and infection of the internal organs can occur [20]. Secondary endogenous infections generally develop after 1 week. Exogenous infection was defined as infection caused by MRSA introduced into the patient from the environment, both animate and inanimate sources. MRSA was transferred directly, omitting the first stage of carriage, to a site where colonisation or infection then occurred, e.g., burn wounds, tracheostomy or gastrostomy. This type of infection can occur at any time during treatment in a PICU [20]. The carriage index was the sum of all semiquantitative MRSA growth densities isolated from surveillance swabs, divided by the total number of swabs taken [18,20].

Analytical methods

Data were collected prospectively and entered into an Access 97 database (Microsoft, Redmond, USA). Prediction of mortality, using the PIM, was calculated on the patient’s first contact with the PICU team [22]. Data included age (months), gender, PIM, underlying diagnosis, length of stay (days), presence or absence of infection, causative microorganism, type of infection, day of infection onset, antimicrobial susceptibility pattern and outcome. Results were expressed as a fraction of the total study population; median and interquartile ranges (IQRs), or mean and standard deviation (SD) or 95% CI were used to describe the demographic distributions. Parametric data were analysed using the Student t-test. Non-parametric data were analysed using the Wilcoxon-Mann-Whitney or Fisher’s exact tests. Correlation was analysed using Pearson’s correlation coefficient. Statistical calculations were performed with SPSS v.11.0.0 (SPSS Inc., Chicago, IL, USA), with p < 0.05 considered to be statistically significant.
RESULTS

Demographics

In total, 1241 patients were included in the study. There were 34 patients positive for MRSA, with a total of 49 admissions during the study period. The male : female ratio was 23 : 11. Median age of the MRSA-positive children was 5.4 months (IQR 2.5–17.7), which was similar to the entire study population (median 3.6 months; IQR 0.5–18.4; p 0.16). Ten children with congenital heart disease were positive for MRSA. Fourteen MRSA patients were medical: five with a respiratory tract infection, two with a chronic neurological condition plus respiratory failure, two with sepsis, two with tracheomalacia, one with laryngeal haemangioma plus respiratory tract infection, one with neurodegenerative disease plus respiratory tract infection, and one with multiple congenital anomalies. Ten MRSA patients were surgical: six children with burns, and four post-surgery. All the children had indwelling devices during their PICU stay: 34 with an endotracheal tube, 29 with a central venous line, 34 with an arterial line, 30 with a urinary catheter, three with a tracheostomy, three with a gastrostomy. The median length of stay was 11 days (IQR 8–21). The 34 MRSA-positive patients were hospitalised for a total of 1030 days. The mean PIM score of this MRSA group was 0.096 (SD 0.105), which was similar to the entire study population (mean PIM 0.108; SD 0.131; p 0.56).

Carriers

There were 29 (2.4%) MRSA carriers among the 1241 patients in the study population. Nineteen children imported MRSA into the unit, nine children acquired MRSA while being treated in the PICU, and one patient was not able to be evaluated. MRSA carriage developed after a median time of 5 days (IQR 4–13). Fifteen patients carried MRSA in the throat only, three solely in rectum, and 11 in throat and rectum. In total, 14 patients received enteral vancomycin, as they were still ventilated in the PICU after detection of the carrier state. MRSA was eradicated in 11 (79%) of these children after a median of 6 days (IQR 3.5–9.75). In two of the remaining three patients, the MRSA carrier load decreased from 5+ to 3+.

Overgrowth

Twenty-two of 29 carriers showed overgrowth (Table 2). The three children who developed five primary endogenous infections belonged to this group. The five primary endogenous infections occurred at a median of 3 days (IQR 1–25) when the level of MRSA was at least 3+, i.e., when the patient was in an overgrowth state. All these children received enteral vancomycin for the eradication of MRSA overgrowth.

Carriage index

The carriage index of the MRSA carrier population was approximately 3+ upon admission, i.e., overgrowth (Fig. 1). The administration of enteral vancomycin reduced the carriage index to <1+ after 2 weeks. There was a steady decline in the carriage index with the commencement of the 5-day course of enteral vancomycin (Fig. 1). The Pearson’s coefficient of correlation (r) was −0.84 (p 0.004).

Table 2. The distribution of MRSA load and its relationship to endogenous infection in critically-ill children treated in a paediatric intensive care unit

<table>
<thead>
<tr>
<th>MRSA load in surveillance cultures</th>
<th>Number of carriers</th>
<th>Primary endogenous infections (five infections in three carriers)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1+</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>2+</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>3+</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>4+</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>5+</td>
<td>15</td>
<td>3</td>
</tr>
</tbody>
</table>

Bold items denote overgrowth [19].

Fig. 1. The impact of enteral vancomycin on the level of MRSA carriage using the carriage index
Infections

During a 4-year period, there were ten (0.8%) patients with 21 MRSA infections; four children with burns, and one each with exomphalos repair plus tracheomalacia, multiple congenital anomalies, chronic lung disease plus bronchiolitis, neurodegenerative disease plus bronchiolitis, pneumonia and laryngeal haemangioma with a tracheostomy. MRSA infection developed after a median period of 8 days (IQR 3–10.5); most were wound infections (14), followed by bloodstream infections (4), and lower airway infections (3). Fifteen (71%) infections were of exogenous pathogenesis and occurred at a median of 8 days (IQR 3–10.5): 11 separate episodes of infection in four burn patients, and one each of septicaemia, exomphalos repair plus tracheomalacia, multiple congenital anomalies, and pneumonia. Five (24%) infections were caused by MRSA present in the flora upon admission of three children (i.e., primary endogenous infection) and occurred at a median of 3 days (IQR 1–25): two septicaemias, one endocarditis, one chest infection and one central venous line infection in a burn patient. The pathogenesis for the remaining infection (laryngeal haemangioma with a tracheostomy) could not be assessed because of an absence of admission surveillance samples. There were no secondary endogenous infections, implying that eradication of MRSA carriers was successful in preventing new infections following transmission via the hands of carers.

DISCUSSION

Five messages emerge from this observational study of 34 children who required ventilation for a minimum period of 4 days: (i) 70% of the patients who carried MRSA carried it in their admission flora; (ii) 79% of the MRSA carriers who received enteral vancomycin cleared MRSA; (iii) MRSA overgrowth was controlled by enteral vancomycin, with subsequent absence of secondary endogenous infections, even though the policy of treating confirmed carriers did not completely prevent transmission; (iv) MRSA infections in the unit were an exogenous problem; (v) there was no emergence of vancomycin resistance, as neither VRE nor VISA were isolated from the 1611 samples.

MRSA was largely a problem of importation into the unit, as 19 of 29 children carried MRSA in their flora upon admission. Surveillance cultures are indispensable for detection of the asymptomatic carrier state, and recent data have demonstrated that a surveillance set should include throat and gut samples, as the digestive tract cannot be ignored [16,17]. Detection of MRSA carriers, both upon admission and later during treatment, is crucial to allow prompt isolation and treatment. Without surveillance, diagnostic samples, including tracheal aspirate, blood, urine and pus, are the only way to detect MRSA in the unit. This traditional approach of taking diagnostic samples results in an inherent and substantial delay which promotes dissemination of MRSA throughout the unit, with consequent endemicity.

The second component of the MRSA control policy was the administration of enteral vancomycin following positive throat and gut cultures. This approach challenges the traditional recommendations of nasal surveillance and topical mupirocin [14,15]. Enteral vancomycin aims to eradicate carriage, or lower the carriage load of MRSA, with two clinical and epidemiological aims [38]: (i) the control of endogenous MRSA infection in an individual patient; and (ii) the control of MRSA dissemination to protect other children in the unit from acquiring MRSA following transmission via the hands of carers.

Overgrowth of potential pathogens including MRSA is a risk-factor for endogenous infection [19,39,40]. MRSA overgrowth was an ‘early’ problem in the unit studied (Fig. 1), in line with the five primary endogenous infections that
occurred at a median of 3 days (Table 2). Once overgrowth was under control, there were no secondary endogenous infections in this study. The use of enteral vancomycin was successful, in that the oropharyngeal gel containing vancomycin (2% w/v) and the vancomycin solution (40 mg/kg/day) administered via a nasogastric tube [28] eradicated or reduced the level of carriage, as demonstrated by the steady decline in the carriage index (Fig. 1). Critically-ill patients are unable to clear abnormal gut flora, including MRSA, because of their underlying disease [41]. Therefore, this decline in MRSA overgrowth reflects an effect of enteral vancomycin treatment, rather than a general improvement in the patients’ health status. Additionally, it is common experience that the traditional use of only parenteral vancomycin fails to clear MRSA from nose, throat, gut and wounds [19,38,42].

Epidemiologically, gut overgrowth promotes the spread of MRSA via hands of carers [18,19,43]. Long-stay patients invariably have overgrowth in their throat and gut, and washing a patient or changing a diaper may lead to contamination of the hands of carers. Eradicating and reducing overgrowth results in a reduction in the overall levels of MRSA density on the skin of patients, and thus a reduced risk of contaminating the hands of carers. In this way, hand-washing becomes more effective in a unit that uses enteral vancomycin. The policy was largely successful, as only nine patients in 4 years acquired MRSA while in the PICU. Enteral vancomycin was administered to confirmed MRSA carriers during the study. The unavoidable delay until surveillance culture results are available means that, for a short period of time, as yet unidentified MRSA carriers are still a potential source of transmission. This factor may have played a role in these nine cases. An alternative preventative approach would be to commence enteral vancomycin treatment immediately for all admitted patients while awaiting the results of admission surveillance samples [19]. Prophylactic vancomycin is recommended only in ICUs with a serious MRSA problem, i.e., one or more infections per week [38]. In the unit described in the present study, where MRSA infection occurs on average only once in 2 months, it is appropriate to use vancomycin only as treatment for carriage.

The profile/risk-factors of the children with MRSA carriage or infection in the unit included burn patients, chronic illness (particularly neurologically impaired children and those with multiple co-morbidities), indwelling devices (including tracheostomies, gastrostomies) and central venous lines. Age and antibiotic regimens did not influence MRSA acquisition in this group. The mortality in this group of children was higher than the background mortality within the PICU, even though the risk of mortality upon admission was similar to the background risk (p 0.56). The number of deaths was too small to project confidently a causal effect.

A particular group of children in this hospital at high risk for exogenous infections are those with burns. Despite repeated investigation and cleansing of the burns unit, MRSA recurred on several occasions following MRSA-free periods. It is suspected that there is transmission from MRSA-positive burn patients seen in the outpatient clinics. MRSA infection in the PICU is mainly an exogenous problem, since the burn patients were MRSA-free upon admission to the PICU and their wounds subsequently became positive for MRSA without previous carriage in throat and gut. Interestingly, most of these patients acquired MRSA while there were no other MRSA-positive patients present in the PICU. This suggests that an external or visiting source may be responsible. High standards of hygiene are crucial to prevent this type of infection. Wounds colonised or infected with MRSA were treated in the PICU with aquaform vancomycin 2% w/v dressing to eradicate exogenous colonisation or infection [19].

Extensive efforts were made during this 4-year study to evaluate 1611 samples for the possibility of colonisation or infection with VRE and VISA in diagnostic samples, and of overgrowth of VRE and VISA in surveillance samples. The failure to detect VRE or VISA, a described concern of an enteral vancomycin protocol [44], may be associated with: (i) the restricted use of enteral vancomycin [45]; (ii) the use of parenteral antimicrobial agents that spare the indigenous flora [24,46]; and (iii) the use of the protocol in an intensive care and hospital setting with no previous isolation of VRE and VISA. Of the 1241 children included in this study, only 14 (1%) received enteral vancomycin, which is hardly indicative of liberal use of vancomycin. Recent published evidence shows that parenteral antimicrobial agents that disturb the patient’s gut ecology, rather than high doses.
of enteral vancomycin, promote the emergence of VRE [27,45,46]. In addition, VRE and VISA are usually imported into an ICU, hence it is not feasible to speculate on the possibility of increasing rates of VRE and VISA. However, the present study is in line with four recent European studies using selective decontamination of the digestive tract, including enteral vancomycin [18–21], none of which reported an increased infection rate with VRE or VISA. These European studies were conducted in ICUs with no history of VRE, although one study detected importation of VRE, but rapid and extensive spread did not occur [19].

In conclusion, surveillance cultures of throat and rectum detected MRSA importation into and transmission within a unit. Enteral vancomycin eradicated the abnormal carrier state of MRSA, and kept PICU patients infection-free without the emergence of VRE and VISA. This novel approach challenges the conventional strategy of nasal surveillance combined with the use of intranasal mupirocin.

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