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Reminder of important clinical lesson

Enteral vancomycin and probiotic use for methicillin-resistant *Staphylococcus aureus* antibiotic-associated diarrhoea

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Summary

A geriatric patient status post intraabdominal surgery presented with persistent diarrhoea and heavy intestinal methicillin-resistant *Staphylococcus aureus* (MRSA) growth after multiple courses of antibiotic therapy. Additionally, swab cultures of the anterior nares tested positive for MRSA. In order to impede infection and prevent future complications, the patient received a 10-day course of vancomycin oral solution 250 mg every 6 h, 15-day course of *Saccharomyces boulardii* 250 mg orally twice daily and a 5-day course of topical mupirocin 2% twice daily intranasally. Diarrhoea ceased during therapy and repeat cultures 11 days after initiating therapy demonstrated negative MRSA growth from the stool and nares. Further repeat cultures 5 months later revealed negative MRSA growth in the stools and minimal MRSA growth in the nares. Overall, enteral vancomycin and probiotics successfully eradicated MRSA infection without intestinal recurrence. Although the results were beneficial treating MRSA diarrhoea for our patient, these agents remain highly controversial.

BACKGROUND

Controversy exists in the literature regarding the use of enteral vancomycin and probiotics to treat methicillin-resistant *Staphylococcus aureus* (MRSA) antibiotic-associated diarrhoea based on the fear of developing resistance versus the spread of infection.

CASE PRESENTATION

An 89-year-old Caucasian man was experiencing diarrhoea during a follow-up visit 2 weeks after the initial admission to a skills/rehabilitation facility. The patient was admitted following a perforated appendix (status post single port laparoscopic appendectomy) where he received multiple courses of intravenous antibiotics including piperacillin/tazobactam, as well as oral amoxicillin/clavulanate and nitrofurantoin. Diarrhoea was initially considered transient based on normal clinical findings and baseline laboratory values/vitals. As a differential diagnosis to rule out medication-induced diarrhoea, a review of his current home and acute medication regimen, including any over-the-counter products or herbals, produced no significant findings. During a follow-up visit 1 week later, the patient continued to experience diarrhoea with new onset general malaise and reduced appetite resulting in weight loss with no dehydration, nausea, vomiting or abdominal pain.

INVESTIGATIONS

Vitals and laboratory results continued to remain within baseline with a white blood cell count of 9.8 cells/mm^3 and a temperature of 36.7°C. Upon physical examination, surgical wounds were healing appropriately and a stool specimen was cultured to rule out infection. Laboratory reports confirmed that the stool culture contained normal enteric flora and heavy growth of MRSA susceptible to clindamycin, linezolid, rifampicin, tigecycline and vancomycin. Additional testing yielded negative results of enterohemorrhagic *Escherichia coli* toxin, *Cryptosporidium* antigen (Ag), *Giardia* Ag, *Shigella* spp., *Campylobacter* spp. and *Clostridium difficile* toxins A and B. The patient was placed on contact precautions, and a swab culture of the anterior nares was additionally performed, which also registered positive for MRSA.

DIFFERENTIAL DIAGNOSIS

It has been well documented that antibiotics place selective pressure on microflora and, as a result, people exposed to antibiotics may develop diarrhoea within 8 weeks of therapy.[1 2] Antibiotic-associated diarrhoea (AAD) has been described as a patient-specific inflammatory infection which ranges in severity from diarrhoea (defined as an increase in frequency of ≥3 bowel movements per day with a decrease in consistency) with no additional complications to debilitating forms, such as colitis.[3 4] Data estimate that AAD affects 3–29% of hospitalised patients receiving antibiotics, but only 33% are diagnosed as *C difficile* infections.[5] Evidence that certain MRSA strains can cause diarrhoea and are enterotoxin-producing demonstrates a need to recognise MRSA as a possible causative agent of AAD.[5 6] Stool specimens testing positive for MRSA establishes MRSA colonisation; however, it does not necessarily indicate MRSA AAD.[5] According to Boyce *et al*[5] the following is necessary to classify MRSA AAD: negative stool assay for *C difficile*, no other identified enteric pathogen, diarrhoea unrelated to medications, heavy growth of MRSA in stool, and little or no normal flora. Additionally, MRSA diarrhoea produces 'greenish' stools in the majority of patients.[5 7] If the diagnosis of MRSA AAD is established, enteral vancomycin may be

the drug of choice since it has been shown to rapidly resolve the infection.[5 7]

TREATMENT

The patient was started on enteral vancomycin 250 mg orally every 6 h for 10 days and mupirocin 2% applied to the anterior nares twice daily for 5 days. In addition, a probiotic (Florastor, Blocodex, Inc., Gentilly, France) 250 mg orally twice daily was prescribed during vancomycin treatment to restore the intestinal flora for 15 days.

OUTCOME AND FOLLOW-UP

Diarrhoea ceased during therapy. Repeat cultures 11 days after the initiation of therapy demonstrated negative MRSA growth from the nares and stool. The patient was released from the rehabilitation facility and discharged to his primary residence. Stool and nares cultures repeated 5 months later demonstrated negative MRSA growth in the stool and mild MRSA colonisation in the nares. Despite the recurrent minimal MRSA colonisation in the nares, the eradication of MRSA from the intestines appears successful in the long term.

DISCUSSION

Antibiotic use

Staphylococcus aureus, a Gram-positive bacteria, is often present in the normal flora of the intestinal tract, skin, and nose of humans.[8] Various organisms with multidrug resistance have been isolated, but none are more prevalent than MRSA.[8] The rates of MRSA infection and colonisation continue to rise particularly among the elderly (age >65 years old), Africans Americans and males.[9] Transmission of MRSA occurs readily in facilities frequented by patients who are carriers (eg, rehabilitation centres, nursing homes and dialysis centres).[10] Colonisation with MRSA should not be considered benign in the elderly since it is associated with increased mortality in nursing home patients.[10]

Once colonised patients are identified in healthcare facilities, the patient is isolated and placed on contact precautions to reduce transmission.[11] Patients heavily colonised in the intestines produce a higher concentration of bacteria on contaminated surfaces and even diligent handwashing may reduce but not eradicate MRSA.[12] Using multiple barrier precautions (eg, gloves, gowns and handwashing) and environmental decontamination has proved beneficial when reducing the transmission of pathogens.[1 13] However, MRSA prevalence continues to increase despite current methods of infection control.[14] The high level of compliance required by healthcare providers, as well as time-constraints and increased costs, may reduce the effectiveness and implementation of infection control procedures in healthcare facilities.[15–17] As a result, other methods may need to be considered to prevent MRSA transmission.

Decolonisation, eradicating MRSA from the source, has become controversial and many question the benefits versus the risk in reducing the prevalence of the bacteria in multiple areas (ie, intestinal regions, nares and topical). The anterior nares are often regarded as the primary site of MRSA colonisation and active surveillance cultures of the nostrils are typically obtained when patients travel between healthcare facilities or hospital wards.[1 18] According to the Infectious Disease Society of America (IDSA),[19] decolonisation strategies, including the application of nasal and topical medications, are not generally recommended unless the colonised patient is experiencing systemic symptoms or experiences recurrent skin and soft tissue infection despite adequate measures. Despite this recommendation, many institutions continue to decolonise patients with nasal and/or topical medications.[20–23] Topical mupirocin 2% is widely regarded as the most effective agent when applied intranasally to decontaminate MRSA nasal carriage; however, recent reports suggest mounting resistance.[8 12 21 24] Intranasal mupirocin 2% as monotherapy should not be used in patients colonised at multiple sites as it has shown poor efficacy at non-nares sites, and patients were significantly more likely to experience persistent colonisation likely due to self-inoculation.[12 25] Therefore, decolonised patients should receive therapy directed at each specific MRSA-positive site.

Current recommendations suggest that surveillance culture of the anterior nares is not enough to identify patients carrying MRSA, as the perianal or rectal region has a higher sensitivity owing to the shedding of the pathogen from stool to skin.[1 14 25 26] Boyce *et al*[11] identified over 150 previously unrecognised patients (MRSA-negative nares culture) with intestinal MRSA colonisation by rectal swab and stool culture. However, routine stool sampling is not recommended and should only be screened when diarrhoea is present.[11]

Intestinal decolonisation, also called intestinal decontamination or Selective Digestive Tract Decontamination (SDD), involves using oral non-absorbed medications to remove a specific pathogen or groups of pathogens cultivating in the intestines to circumvent the possibility of future infections in high-risk patients.[1] Regimens historically contain agents impeding Gram-negative and fungal organisms that significantly reduced endogenous infections compared to oropharyngeal decontamination and standard care.[14 27] However, SDD remains controversial.[28 29] A 2003 Cochrane review of six studies found no benefit in using oral antimicrobials for routine decolonisation and suggested that there may be adverse reactions from systemic agents including rifampin and trimethoprim-sulfamethoxazole (TMP-SMX).[20] Consequently, the IDSA recommends oral agents only for active infections of MRSA and suggests combining rifampin with doxycycline or TMP-SMX.[19]

Recently, proponents of SDD have recommended the addition of enteral vancomycin to the SDD regimen in order to eliminate the primary source of colonisation leading to endogenous MRSA infections in at-risk patients and reduce transmission to other patients.[12 14] Enteral vancomycin is rarely absorbed in the blood, thereby providing a higher concentration in the stool and a means to eliminate MRSA from the intestinal flora.[30] Multiple studies have demonstrated that the use of enteral vancomycin in eradicating MRSA from the intestines is safe and effective in various patient populations.[5 12 24 26 29 30]

On the contrary, the Hospital Infection Control Practices Advisory Committee, in collaboration with the Centre for Disease Control and Prevention, specifically recommend against the use of oral vancomycin in SDD to limit the emergence of vancomycin-resistant enterococci (VRE) and vancomycin-intermediate *S aureus* (VISA).[29] Additional

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opponents of enteral vancomycin in accordance with SDD suggest that decolonisation may exacerbate antibiotic resistance.[18–20 31–33] Intravenous agents, including vancomycin, produce fluctuating faecal concentrations following bilary excretion.[28 29] Therefore, resistance may be formed in the intestine by the presence of low antibiotic concentration, which eliminates sensitive flora leading to overgrowth of antibiotic-resistant organisms.[28 29] A meta-analysis concluded that prior exposure to the intravenous use of vancomycin (but not oral) is modestly associated with VRE colonisation.[13 15 24] Additionally, studies involving two colonised MRSA patients with concurrent *C difficile* infections reported incomplete eradication of MRSA and an increase in VRE concentrations after therapy with enteral vancomycin 125 mg every 6 h.[18 34] Even though these studies used a vancomycin dosing regimen that was therapeutic for *C difficile* infections it did not produce the intended effect.[35] Alternatively, studies that orally administered 2 g/day of vancomycin provided complete eradication of MRSA and failed to substantiate any resistance.[12 28] The absence of resistance may be explained by the high faecal concentration produced from utilising 2 g/day of enteral vancomycin, which far exceeds the minimum-bactericidal concentration of VISA and VRE.[26] Some disregarded the lack of resistance reported in such studies as short-term effects that did not account for the development of resistance over time. However, recent long-term prospective studies demonstrate that enteral vancomycin does not produce de novo development of VRE or VISA resistance and may be considered as a treatment option in vulnerable populations (eg, elderly).[14 26 28]

Eliminating MRSA from the intestines or nares is not always cited as successful or long lasting. One study demonstrated that 48% of those who underwent nares decolonisation were culture positive after 6 months.[31] Many proponents of giving enteral vancomycin for SDD cite the recurrence rates; however, recurrence varied greatly by the dosing regimens. In addition to those studies administering 2 g/day, Maraha *et al*[24] completely eradicated MRSA colonisation in all subjects and demonstrated a lack of recurrence during a 1-year follow-up period with a regimen of oral vancomycin solution 250 mg every 6 h for 5 days, topical intranasal mupirocin 2%, bathes with povidone-iodine shampoo, along with strict isolation and barrier precautions until two consecutive negative MRSA cultures were obtained.

When evaluating our case, active surveillance measures were not conducted when our patient was transferred from the hospital to the rehabilitation centre. Therefore, the stool culture for the persistent diarrhoea was the primary means of determining that our patient was colonised with MRSA. Isolation methods and barrier protections were initiated appropriately after the positive MRSA stool culture; however, active surveillance cultures of nares and perianal swabs should have been utilised to reduce subsequent hand contamination with MRSA. Since surveillance cultures were not performed and the patient was not previously classified as an MRSA carrier, the origin of the transmission of MRSA is unknown. We hypothesise that the patient contracted MRSA in the hospital ward and the heavy growth of MRSA predominated with antibiotic use. During the 8 weeks postantibiotic use, persistent diarrhoea (≥14 days) led us to consider the possibility of AAD. In light of the evidence of heavy MRSA growth and negative results of other causative pathogens including *C difficile*, we felt that the patient was infected with MRSA AAD.

The decision to treat our patient with enteral vancomycin was multifaceted. Owing to an age >65, an increased risk for systemic infection from recent intestinal surgery (in which the appendix was perforated), and the need to reduce transmission to other patients, we decided to treat the patient with enteral vancomycin and topical intranasal mupirocin 2%. From past experience in treating *C difficile* infections and studies that demonstrated enteral vancomycin is safe and effective, it was extrapolated that enteral vancomycin may be sufficient in removing the MRSA pathogenic cause of diarrhoea and prevent possible endogenous infections. The dosing regimen utilised (250 mg orally every 6 h) was based on the success of Maraha *et al*, which completely eliminated MRSA colonisation and prevented recurrence.[24] However, it appears that 2 g/day (500 mg orally every 6 h) may be a better treatment option based on the majority of clinical trials using this higher dosage.[12 26 28–30] The patient did experience recurrent MRSA colonisation in the nares 5 months after therapy, which is consistent with previous data suggesting almost 50% recurrence rate 6 months later.[31] However, since no additional complications are present and he has returned to living independently, the nares colonisation will not be treated at this time. Overall, oral vancomycin therapy effectively eradicated MRSA from the intestines, as demonstrated by two negative MRSA stool cultures 11 days and 5 months after the initiation of therapy, from a high-risk patient. Although controversy exists, we offer additional evidence supporting the use of enteral vancomycin for MRSA AAD in high-risk patients.

Probiotic use

Probiotics, which contain live, non-pathogenic bacteria or yeast, may restore and maintain microbial balance in the intestines after antibiotic use.[36] Multiple meta-analyses determined that concurrent administration of probiotics with antibiotics resulted in a reduced frequency of diarrhoea.[37] The American College of Gastroenterology also recommends probiotics in the treatment regimen of AAD.[38] While multiple probiotics are available, *Saccharomyces boulardii* (Florastor) provides the strongest evidence and may additionally prevent AAD recurrence when administered with high-dose oral vancomycin (2 g/day).[36 37]

Whereas data appear to support the use of probiotics, their use in AAD therapeutic regimens is also controversial. Some national guidelines and organisations (eg, IDSA and Society for Healthcare Epidemiology of America) are cautious about recommending an agent which is not considered a drug.[36 39] Probiotics are currently considered dietary supplements by most countries and do not fall under the same regulations as prescription medications.[39] Some probiotic agents, such as Florastor, are manufactured by established pharmaceutical companies with quality-controlled protocols. However, other probiotic agents contain fluctuating concentrations and microorganism strains different from that stated on the label.[37] Additionally, probiotics are highly contraindicated in high-risk populations (eg, immunocompromised, critically ill and central venous catheter) owing to the increased

risk for developing fungemia and bacteraemia.[36 39] However, postmarketing studies have demonstrated that probiotics appear to be safe with mild tolerable side effects (eg, bloating, flatulence, constipation and thirst) in non-high-risk populations.[36 39]

Our patient did not meet the criteria for a patient at high risk of developing fungaemia. Furthermore, we felt that our patient would benefit from the supporting evidence that *S boulardii* may reduce the frequency of diarrhoea and AAD recurrence. This led us to administer *S boulardii* (Florastor) 250 mg orally twice daily for a 15-day course with concurrent oral vancomycin.

Learning points

- Vulnerable patient populations for methicillin-resistant *Staphylococcus aureus* (MRSA) colonisation and infection include: elderly, males, African Americans and those in facilities frequented by multiple patients (eg, rehabilitation centres and nursing homes).
- A stool culture positive for MRSA without any identifiable antibiotic-associated diarrhoea (AAD) characteristics may represent colonisation and does not warrant therapy.
- MRSA AAD is typically characterised by diarrhoea unrelated to medications, recent antibiotic use (within 8 weeks), negative stool assay for *Clostridium difficile*, no other identified enteric pathogen, heavy growth of MRSA in stool and little or no normal flora.
- Recent data suggest that treatment with oral vancomycin (500 mg by mouth every 6 h) does not demonstrate multidrug resistance and appears to be a safe and effective treatment in MRSA AAD when used appropriately.
- Caution is warranted when using topical mupirocin 2% to treat MRSA nares colonisation, since studies suggest it may cause resistance and recurrence (~50%) of MRSA colonisation in the nares.
- Probiotic use (eg, *Saccharomyces boulardii* 250–500 mg orally twice daily) may be beneficial in select patient populations when given concurrently with antibiotics. However, caution is warranted as these agents are considered as supplements and not regulated as drugs.

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REFERENCES

1. **Donskey CJ.** The role of the intestinal tract as a reservoir and source for transmission of nosocomial pathogens. *Clin Infect Dis* 2004;**39**:219–26.
2. **McFarland LV.** Antibiotic-associated diarrhea: epidemiology, trends and treatment. *Future Microbiol* 2008;**3**:563–78.
3. **Guerrant RL,** Van Gilder T, Steiner TS, *et al*. Practice guidelines for the management of infectious diarrhea. *Clin Infect Dis* 2001;**32**:331–50.
4. **Bartlett JG.** Antibiotic-associated diarrhea. *N Engl J Med* 2002;**346**:334–9.
5. **Boyce JM,** Havill NL. Nosocomial antibiotic-associated diarrhea associated with enterotoxin-producing strains of methicillin-resistant *Staphylococcus aureus*. *Am J Gastroenterol* 2005;**100**:1828–34.
6. **Gravet A,** Rondeau M, Harf-Monteil C, *et al*. Predominant *Staphylococcus aureus* isolated from antibiotic-associated diarrhea is clinically relevant and produces enterotoxin A and the bicomponent toxin LukE-lukD. *J Clin Microbiol* 1999;**37**:4012–19.
7. **Lo TS,** Borchardt SM. Antibiotic-associated diarrhea due to methicillin-resistant *Staphylococcus aureus*. *Diagn Microbiol Infect Dis* 2009;**63**:388–9.
8. **APIC.** Guide to the elimination of methicillin-resistant Staphylococcus aureus (MRSA) transmission in hospital settings, 2nd edn. 2010. http://www.apic.org/Resource_/EliminationGuideForm/631fcd91–8773–4067-9f85-ab2a5b157eab/File/MRSA-elimination-guide-2010.pdf (accessed 24 Mar 2012).
9. **APIC.** Guide to the elimination of methicillin-resistant Staphylococcus aureus (MRSA) transmission in long-term care facility. 2009. http://www.apic.org/Resource_/EliminationGuideForm/08b12595-9f92-4a64-ad41-4afdd0088224/File/APIC-MRSA-in-Long-Term-Care.pdf (accessed 24 Mar 2012).
10. **Baldwin NS,** Gilpin DF, Hughes CM, *et al*. Prevalence of methicillin-resistant *Staphylococcus aureus* colonization in residents and staff in nursing homes in Northern Ireland. *J Am Geriatr Soc* 2009;**57**:620–6.
11. **Boyce JM,** Havill NL, Maria B. Frequency and possible infection control implications of gastrointestinal colonization with methicillin-resistant *Staphylococcus aureus*. *J Clin Microbiol* 2005;**43**:5992–5.
12. **Silvestri L,** Milanese M, Oblach L, *et al*. Enteral vancomycin to control methicillin-resistant *Staphylococcus aureus* outbreak in mechanically ventilated patients. *Am J Infect Control* 2002;**30**:391–9.
13. **Safdar N,** Maki DG. The commonality of risk factors for nosocomial colonization and infection with antimicrobial-resistant *Staphylococcus aureus*, enterococcus, gram-negative bacilli, *Clostridium difficile*, and *Candida*. *Ann Intern Med* 2002;**136**:834–44.
14. **van Saene HKF,** Weir WI, de la Cal MA, *et al*. Enteral vancomycin to control MRSA. *J Hosp Infect* 2005;**59**:263–6.
15. **Gerding DN.** Is there a relationship between vancomycin-resistant enterococcal infection and *Clostridium difficile* infection? *Clin Infect Dis* 1997;**25**(Suppl 2):S206–10.
16. **Larssen KW,** Jacobsen T, Bergh K, *et al*. Outbreak of methicillin-resistant *Staphylococcus aureus* in two nursing homes in Central Norway. *J Hosp Infect* 2005;**60**:312–6.
17. **Rodríguez-Baño J,** García L, Ramírez E, *et al*. Long-term control of endemic hospital-wide methicillin-resistant *Staphylococcus aureus* (MRSA): the impact of targeted active surveillance for MRSA in patients and healthcare workers. *Infect Control Hosp Epidemiol* 2010;**31**:786–95.
18. **Ray AJ,** Pultz NJ, Bhalla A, *et al*. Coexistence of vancomycin-resistant enterococci and *Staphylococcus aureus* in the intestinal tracts of hospitalized patients. *Clin Infect Dis* 2003;**37**:875–81.
19. **Liu C,** Bayer A, Cosgrove SE, *et al*. Clinical practice guidelines by the Infectious Diseases Society of America for the treatment of methicillin-resistant *Staphylococcus aureus* infections in adults and children. *Clin Infect Dis* 2011;**52**:e18–55.
20. **Loeb MB,** Main C, Eady A, *et al*. Antimicrobial drugs for treating methicillin-resistant *Staphylococcus aureus* colonization. *Cochrane Database Syst Rev* 2003;**4**:CD00340.
21. **Patel JB,** Gorwitz RJ, Jernigan JA. Mupirocin resistance. *Clin Infect Dis* 2009;**49**:935–41.
22. **Robicsek A,** Beaumont JL, Paule SM, *et al*. Universal surveillance for methicillin-resistant *Staphylococcus aureus* in 3 affiliated hospitals. *Ann Intern Med* 2008;**148**:409–18.
23. **Mody L,** Kauffman CA, McNeil SA, *et al*. Mupirocin-based decolonization of *Staphylococcus aureus* carriers in residents of 2 long-term care facilities: a randomized, double-blind, placebo-controlled trial. *Clin Infect Dis* 2003;**37**:1467–74.
24. **Maraha B,** van Halteren J, Verzijl JM, *et al*. Decolonization of methicillin-resistant *Staphylococcus aureus* using oral vancomycin and topical mupirocin. *Clin Microbiol Infect* 2002;**8**:671–5.
25. **Squier C,** Rihs JD, Risa KJ, *et al*. *Staphylococcus aureus* rectal carriage and its association with infections in patients in a surgical intensive care unit and a liver transplant unit. *Infect Control Hosp Epidemiol* 2002;**23**:495–501.
26. **de la Cal MA,** Cerdá E, van Saene HKF, *et al*. Effectiveness and safety of enteral vancomycin to control endemicity of methicillin-resistant *Staphylococcus aureus* in a medical/surgical intensive care unit. *J Hosp Infect* 2004;**56**:175–83.
27. **Silvestri L,** van Saene HKF, Milanese M, *et al*. Selective decontamination of the digestive tract reduces bacterial bloodstream infection and mortality in critically ill patients: systematic review of randomized, controlled trials. *J Hosp Infect* 2007;**65**:187–203.
28. **Ochoa-Ardila ME,** García-Cañas A, Gómez-Mediavilla K, *et al*. Long-term use of selective decontamination of the digestive tract does not increase antibiotic resistance: a 5-year prospective cohort study. *Intensive Care Med* 2011;**37**:1458–65.
29. **Silvestri L,** van Saene HKF, Milanese M, *et al*. Prevention of MRSA pneumonia by oral vancomycin decontamination: a randomised trial. *Eur Respir J* 2004;**23**:921–6.

30. **Konishi T,** Idezuki Y, Kobayashi H, *et al*. Oral vancomycin hydrochloride therapy for postoperative methicillin-cephem-resistant *Staphylococcus aureus* enteritis. *J Surg* 1997;**27**:826–32.
31. **Muto CA,** Jernigan JA, Ostrowsky BE, *et al*. SHEA guideline for preventing nosocomial transmission of multidrug-resistant strains of *Staphylococcus aureus* and *Enterococcus*. *Infect Control Hosp Epidemiol* 2003;**24**:362–86.
32. **Daschner F.** MRSA: really time for a more pragmatic approach? *J Hosp Infect* 2005;**59**:259; author reply 63–6.
33. **Quigley EM.** Passing the bug-translocation, bacteremia, and sepsis in the intensive care unit patient: is intestinal decontamination the answer? *Crit Care Med* 2011;**39**:1202–3.
34. **Bhalla A,** Aron DC, Donskey CJ. *Staphylococcus aureus* intestinal colonization is associated with increased frequency of *S. aureus* on skin of hospitalized patients. *BMC Infect Dis* 2007;**7**:105–11.
35. **Cohen SH,** Gerding DN, Johnson S, *et al*. Clinical practice guidelines for *Clostridium difficile* infection in adults: 2010 update by the Society for Healthcare Epidemiology of America (SHEA) and the Infectious Diseases Society of America (IDSA). *Infect Control Hosp Epidemiol* 2010;**31**:431–55.
36. **Williams NT.** Probiotics. *Am J Health Syst Pharm* 2010;**67**:449–58.
37. **McFarland LV.** Evidence-based review of probiotics for antibiotic-associated diarrhea and *Clostridium difficile* infections. *Anaerobe* 2009;**15**:274–80.
38. **Avadhani A,** Miley H. Probiotics for prevention of antibiotic-associated diarrhea and *Clostridium difficile*-associated disease in hospitalized adults-A meta-analysis. *J Am Acad Nurse Pract* 2011;**23**:269–74.
39. **Venugopalan V,** Shriner KA, Wong-Beringer A. Regulatory oversight and safety of probiotic use. *Emerg Infect Dis* 2010;**16**:1661–5.