originated (data not shown), one would perhaps expect to see mutations being lost or gained within the genes potentially affecting quinolone susceptibility. The stability of mutations in genes known to be associated with fluoroquinolone resistance, and the stable MIC values in clonally related MRSA isolates over time, have important implications for quinolone resistance in *S. aureus*. From this study of clinical MRSA isolates, it seems likely that once acquired, mutations and the decreased susceptibility to quinolones that they confer are highly stable, suggesting that the high prevalence of fluoroquinolone resistance that we are experiencing today in some parts of the world will remain.

References

1. Goldstein FW, Acar JF. Epidemiology of quinolone resistance: Europe and North and South America. Drugs 1995; 49 (suppl 2): 36–42.
2. Kaatz GW, Seo SM. Inducible *norA*-mediated multidrug resistance in *Staphylococcus aureus*. Antimicrob Agents Chemother 1995; 39: 2650–5.
3. Yoshida H, Bogaki M, Nakamura S, Ubukata K, Konno M. Nucleotide sequence and characterization of the *Staphylococcus aureus norA* gene which confers resistance to quinolones. J Bacteriol 1990; 172: 6942–9.
4. Brockbank SMV, Barth PT. Cloning, sequencing, and expression of the DNA gyrase genes from *Staphylococcus aureus*. J Bacteriol 1993; 175: 3269–77.
5. Goswitz JJ, Willard KE, Fashing CE, Peterson LR. Detection of *gyrA* gene mutations associated with ciprofloxacin resistance in methicillin resistant *Staphylococcus aureus*: Analysis by polymerase chain reaction and automated DNA sequencing. Antimicrob Agents Chemother 1992; 36: 1166–9.
6. Ito H, Yoshida H, Bogaki-Shonnai M, Niga T, Hattori H, Nakamura S. Quinolone resistance mutations in the DNA gyrase *gyrA* and *gyrB* genes of *Staphylococcus aureus*. Antimicrob Agents Chemother 1994; 38: 2014–23.
7. Margerrison EEC, Hopewell R, Fisher LM. Nucleotide sequence of the *Staphylococcus aureus gyrB–gyrA* locus encoding the DNA gyrase A and B proteins. J Bacteriol 1992; 174: 1596–603.
8. Takenouchi T, Ishii C, Sugawara M, Tokue Y, Ohya S. Incidence of various *gyrA* mutations in 451 *Staphylococcus aureus* strains isolated in Japan and their susceptibilities to 10 fluoroquinolones. Antimicrob Agents Chemother 1995; 39: 1414–18.
9. Ferrero L, Cameron B, Manse B, et al. Cloning and primary structure of *Staphylococcus aureus* DNA topoisomerase IV: primary target of fluoroquinolones. Mol Microbiol 1994; 13: 641–53.
10. Takahata M, Yonezawa, M, Kurose S, et al. Mutations in the *gyrA* and *grlA* genes of quinolone-resistant clinical isolates of methicillin-resistant *Staphylococcus aureus*. J Antimicrob Chemother 1996; 38: 543–6.
11. Yamagishi, JI, Kojima T, Oyamada Y, et al. Alterations in the DNA topoisomerase IV *grlA* gene responsible for quinolone resistance in *Staphylococcus aureus*. Antimicrob Agents Chemother 1996; 40: 1157–63.
12. Blanche F, Cameron B, Bernard FX, et al. Differential behaviours of *Staphylococcus aureus* and *Escherichia coli* type II DNA topoisomerases. Antimicrob Agents Chemother 1996; 40: 2714–20.
13. Ferrero L, Cameron B, Crouzet J. Analysis of *gyrA* and *grlA* mutations in stepwise-selected ciprofloxacin-resistant mutants of *Staphylococcus aureus*. Antimicrob Agents Chemother 1995; 39: 1554–8.
14. Ng EY, Trucksis M, Hooper DC. Quinolone resistance mutations in topoisomerase IV: relationship to the *flqA* locus and genetic evidence that topoisomerase IV is the primary target and DNA gyrase is the secondary target of fluoroquinolones in *Staphylococcus aureus*. Antimicrob Agents Chemother 1996; 40: 1881–8.
15. Schmitz FJ, Steiert M, Tichy HV, et al. Typing of methicillin-resistant *Staphylococcus aureus* isolates from Düsseldorf by six genotypic methods. J Med Microbiol 1998; 47: 341–51.
16. Schmitz FJ, Hofmann B, Verhoef J, et al. Specific information concerning taxonomy, pathogenicity and methicillin resistance of staphylococci obtained by a Multiplex PCR. J Med Microbiol 1997; 46: 773–8.
17. National Committee for Clinical Laboratory Standards. Methods for dilution antimicrobial tests for bacteria that grow aerobically. M7-A2. Villa Nova, Pa: NCCLS, 1991.
18. Hori S, Ohshita Y, Utsui Y, Hiramatsu K. Sequential acquisition of norfloxacin and ofloxacin resistance by methicillin-resistant and -susceptible *Staphylococcus aureus*. Antimicrob Agents Chemother 1993; 37: 2278–84.
19. Schmitz F-J, Jones ME, Hofmann B, et al. Characterisation of *grlA*, *grlB*, *gyrA* and *gyrB* mutations in 116 unrelated isolates of *Staphylococcus aureus* and effects of mutations on ciprofloxacin MIC. Antimicrob Agents Chemother 1998; 42: 1249–52.
20. Schmitz F-J, Hertel B, Hofmann B, et al. Relationship between mutations in the coding and promoter regions of the *norA* genes in 42 unrelated clinical isolates of *Staphylococcus aureus* and the MICs of norfloxacin for these strains. J Antimicrob Chemother 1998; 42: 561–3.

Lactobacillus endocarditis caused by a probiotic organism

Andrew D. Mackay[1], Mark B. Taylor[2], Christopher C. Kibbler[3] and Jeremy M. T. Hamilton-Miller[4]

[1]Department of Medical Microbiology, University College Hospital, [2]Department of Medical Microbiology, Royal London Hospital Medical College, [3]Department of Medical Microbiology, Royal Free Hampstead NHS Trust & Royal Free and University College Medical School and [4]Department of Medical Microbiology, Royal Free and University College Medical School, Royal Free Campus, Rowland Hill Street, London, NW3 2PF, UK

Tel: +44 171 749 0500   Fax: +44 171 435 9694   E-mail: j.hamilton-miller@rfhsm.ac.uk

Accepted 17 September 1998

Probiotics are microorganisms deliberately ingested to modify the gut flora in order to produce 'health' [1]. We report here what we believe to be the first case of endocarditis due to *Lactobacillus rhamnosus* brought about by self-medication with a freeze-dried probiotic preparation, in a subject who was previously fit and well.

Lactobacillus spp. are universally found in the mouth, female genital tract and gastrointestinal tract of humans, as well as in many foods and health food preparations. They are generally considered to be non-pathogenic [2,3]. Large quantities of products containing lactobacilli are sold worldwide; for example, 3×10^6 kg of products containing *Lactobacillus* sp. GG (ATCC 53103) were sold in Finland alone in 1992 [2]. However, lactobacilli have been associated causally with endocarditis, meningitis, pneumonia and local suppurative conditions [4]. The case of endocarditis we report is also interesting since the source of the infecting bacteria in endocarditis is so rarely elucidated. (This case was presented as Poster M243 at The Second European Congress of Chemotherapy, Hamburg, May 1998.)

A 67-year-old male with previously documented mild mitral valve regurgitation due to mitral valve prolapse presented to his family doctor complaining of persistent dry cough, slight shortness of breath and weight loss. A few weeks earlier, some carious teeth had been removed, and 3 g of amoxycillin by mouth 1 h before the procedure was given as prophylaxis. The subject was taking one or two capsules daily of a freeze-dried probiotic preparation, each capsule of which was stated to contain 2×10^9 *L. rhamnosus* and several other bacterial species (including *L. acidophilus* and *Streptococcus faecalis*) to provide 'a spectrum of friendly bacteria that inhabit the healthy gut'. As the subject had found the capsules too large to swallow, he was in the habit of emptying their contents into his mouth and chewing them with milk.

The subject was referred to hospital; on examination, he looked well. Old splinter hemorrhages were present on one hand. He was apyrexial, with blood pressure 140/90 mmHg and pulse 90/min in sinus rhythm. A loud pansystolic murmur of mitral valve

regurgitation was present at the cardiac apex, radiating to his axilla. His lungs were clear and there were no signs of heart failure. The remainder of the examination was unremarkable. Results of laboratory tests were normal apart from low hemoglobin (111 g/L), and raised C-reactive protein (22 mg/L) and erythrocyte sedimentation rate (ESR) (52 mm/h). Chest X-ray and electrocardiogram were normal. A transthoracic echocardiogram showed moderate mitral valve regurgitation and increased tissue on the posterior mitral valve leaflet which was thought to be a small vegetation.

Blood cultures yielded Gram-positive rods in all bottles of three sets. These grew in short chains on solid media after 48 h, and were catalase negative, aesculin positive and non-motile; further testing by API 50CHL and at The Public Health Laboratory showed the organisms to be *L. rhamnosus*. Eight further sets of blood cultures were also positive for *L. rhamnosus*. The antibiotic sensitivity was as shown in Table 1. One of the organisms cultured from the probiotic capsules was indistinguishable from that isolated from the blood cultures by virtue of identical cultural appearance, reactions in API 50CHL, sensitivity patterns and pyrolysis mass spectrometry.

The patient was treated with intravenous ampicillin (2 g 8-hourly)+gentamicin (80 mg 12-hourly) for 2 weeks and was discharged, well, on pivampicillin (1 g 12-hourly)+probenecid (500 mg 6-hourly) for 6 weeks. Attempts to isolate the causal lactobacillus from the patient's teeth or bowel were unsuccessful. The patient was well at follow-up 3 months after admission.

Although lactobacilli are recognized to be of low intrinsic virulence, there are several reports of infection caused by members of this genus. There are at least 58 cases of endocarditis in the literature [5–8]; 50% of these patients had some form of dental disease or had had dental treatment prior to the onset of endocarditis. Further, Antony et al [9] described 55 patients with lactobacillus bacteremia (often as part of a polybacteremia) in the absence of endocarditis. In those cases where etiologic strains were speciated (unfortunately, this was often not done), it is clear that the great

Table 1 Susceptibility pattern of *Lactobacillus rhamnosus* (MICs in mg/L)

Sensitive	Intermediate	Resistant
Chloramphenicol (<4)	Ampicillin (2)	Cephaloridine (32)
Clindamycin (<0.12)	Benzylpenicillin (0.5)	Co-trimoxazole (4/76[a])
Erythromycin (<0.12)		Vancomycin (128)
Gentamicin (2)		
Imipenem (2)		
Rifampicin (<1)		
Tetracycline (2)		

[a]Trimethoprim/sulfamethoxazole.

majority were the closely related, vancomycin-resistant [10] species *L. casei*, *L. paracasei* or *L. rhamnosus*, and that the vancomycin-sensitive species *L. acidophilus* is only rarely implicated.

Probiotics appear to be attractive to the public; promotional material makes such claims as 'maintains a healthy digestion', 'improves digestibility and assimilation of food', 'keeps intestinal contents sweet', 'assists general well-being', and 'protects skin against harmful microbes'. As, in the UK, probiotics are foods rather than medicines, this type of claim, although virtually impossible to substantiate, is allowed.

There is considerable evidence that lactobacilli may be tolerant to β-lactam antibiotics [6,11]; this may have led to the failure in the case reported here of the oral prophylaxis given before the dental treatment. Tolerance has also been held responsible for treatment failure in several cases [6]. The patient described here chewed the contents of capsules, which could have increased the risk of endocarditis following dental treatment. Patients who are immunosuppressed or have pre-existing heart valve disease should avoid probiotic preparations containing *L. rhamnosus*, and warnings on packaging to this effect should be considered. It is noticeable that in the case presently being discussed, it was the *L. rhamnosus* rather than the other constituents of the probiotic capsules that caused the endocarditis, although all the species present had equal opportunity to colonize the valve. There appears to be less risk attached to the use of probiotic organisms such as *L. acidophilus* (see above) or *Lactobacillus* sp GG [2]. Another probiotic species best avoided is *Enterococcus faecium* (especially if vancomycin resistant [12]), as there may be more risks than benefits from its use [13].

References

1. Fuller R (ed.). Probiotics. The scientific basis. London: Chapman & Hall, 1992.
2. Saxelin M, Chuang N, Chassy B, et al. Lactobacilli and bacteremia in Southern Finland, 1989–1992. Clin Infect Dis 1996; 22: 564–6.
3. Adams MR, Marteau P. On the safety of lactic acid bacteria from food. Int J Food Microbiol 1995; 27: 263–4.
4. Aguirre M, Collins MD. Lactic acid bacteria and human clinical infection. J Appl Bacteriol 1993; 75: 95–107.
5. Sussman JI, Baron EJ, Goldberg SM, Kaplan MH, Pizzarello RA. Clinical manifestations and therapy of lactobacillus endocarditis: report of a case and review of the literature. Rev Infect Dis 1986; 8: 771–6.
6. Griffiths JK, Daly JS, Dodge RA. Two cases of endocarditis due to lactobacillus species: antimicrobial susceptibility, review, and discussion of therapy. Clin Infect Dis 1992; 15: 250–5.
7. Husni RN, Gordon SM, Washington JA, Longworth DL. Lactobacillus bacteremia and endocarditis: review of 45 cases. Clin Infect Dis 1997; 25: 1048–55.
8. Harty DWS, Patrikakis M, Knox KW. Identification of lactobacillus strains isolated from patients with infective endocarditis and comparison of their surface-associated properties with those of other strains of the same species. Microb Ecol Hlth Dis 1993; 6: 191–201.
9. Antony SJ, Stratton CW, Dummer JS. Lactobacillus bacteremia: description of the clinical course in adult patients without endocarditis. Clin Infect Dis 1996; 23: 773–8.
10. Hamilton-Miller JMT, Shah S. Vancomycin susceptibility as an aid to the identification of lactobacilli. Lett Appl Microbiol 1998; 26: 153–4.
11. Hamilton-Miller JMT, Shah S. Susceptibility patterns of vaginal lactobacilli to eleven oral antibiotics. J Antimicrob Chemother 1994; 33: 1059–60.
12. Alcid DV, Troke M, Andszewski S, John JF. Probiotics as a source of *Enterococcus faecium*. Abstracts of the Infectious Diseases Society of America Meeting, 1994: 123.
13. Hamilton-Miller JMT, Shah S. Benefits and risks of *Enterococcus faecium* as a probiotic. In Sadler MJ, Saltmarsh M, eds. Functional foods: the consumer, the products and the evidence. London: Royal Society of Chemistry, 1998: 20–4.

High genetic identity within the C:2b:P1.2,5 meningococcal epidemic strain in Galicia (Spain)

L. Arreaza[1], S. Berrón[1], J. A. Gómez[2], M. I. Sánchez-Romero[3], S. Fernández[4], M. I. Santiago[4] and J. A. Vázquez[1]*

[1]Laboratorio de Referencia de Meningococos, Centro Nacional de Microbiología, Instituto de Salud Carlos III, 28220 Majadahonda, Madrid, [2]Departmento Microbiología, Facultad de Farmacia, Universidad de Santiago, Santiago de Compostela, A Coruña, [3]Servicio de Microbiología, Hospital de la Princesa, Madrid, and [4]Dirección Xeral de Saúde Pública, Xunta de Galicia, Santiago de Compostela, A Coruña, Spain

*Tel: +39 509 7901   Fax: +39 509 7966   E-mail: jvazquez@isc111.es

Accepted 3 November 1998

In the early 1990s, an increasing number of serogroup C meningococcal strains was observed [1], and a rise in the incidence of the disease was also found, especially in some regions in the northwest of the country,