

Enterococcus spp bacteraemia: England, Wales, and Northern Ireland: 2003

Key points:

- In 2003 there were 6036 reports of *Enterococcus* spp bacteraemia, a 20% increase on 2002.
- Reporting of antibiotic susceptibility improved in 2003 compared to 2002.
- The percentage of glycopeptide-resistant isolates either remained constant or declined between 2002 and 2003, depending on the species and antibiotic.
- Possible misidentification of enterococci can be detected by examination of reported resistance patterns, particularly ampicillin/amoxycillin and quinupristin/dalfopristin.

Introduction

This report describes *Enterococcus* spp (including Group D streptococci) isolated from specimens in 2003 by laboratories in England, Wales, and Northern Ireland and voluntarily reported to the Health Protection Agency's Centre for Infections via CoSurv (1). Age- and region-specific rates were calculated using 2003 mid-year population estimates. Where the percentage resistance to a specific antibiotic is given, the denominator excludes those reports without susceptibility information for that antibiotic. Confidence intervals were calculated using STATA†.

In 2003 there were 6036 reports (table 1) of *Enterococcus* spp bacteraemia (including Group D streptococci). Of these, 2647 reports indicated *E. faecalis* (44%) and 1011 reports indicated *E. faecium* (17% of the total). Thirty-two per cent of the isolates reported were not identified beyond the genus. Four per cent (216 reports) indicated Group D streptococci. *E. faecalis* accounted for 65% and *E. faecium* 25% of the reports that included the species name. Of the 217 laboratories in England, Wales, and Northern Ireland, 182 (84%) reported at least one *Enterococcus* spp bacteraemia in 2003 (table 2). Of these 182 laboratories, 164 (90%) included susceptibility information for enterococci.

Table 1 Laboratory reports of *Enterococcus* spp bacteraemia: England, Wales, and Northern Ireland: 2003

<i>Enterococcus</i> spp	Number of reports
<i>Enterococcus</i> not fully identified	1955
<i>Enterococcus avium</i>	36
<i>Enterococcus casseliflavus</i>	21
<i>Enterococcus durans</i>	49
<i>Enterococcus faecalis</i>	2647
<i>Enterococcus faecium</i>	1011
<i>Enterococcus gallinarum</i>	92
<i>Enterococcus hirae</i>	4
<i>Enterococcus raffinosus</i>	5
Streptococci group D	216
Total	6036

The reporting rate for *Enterococcus* spp bacteraemia for England, Wales, and Northern Ireland combined was 11.9 per 100,000 population (figure 1). Region-specific rates ranged from 15.3/100,000 in Yorkshire and Humberside, to 8.2/100,000 in the South East.

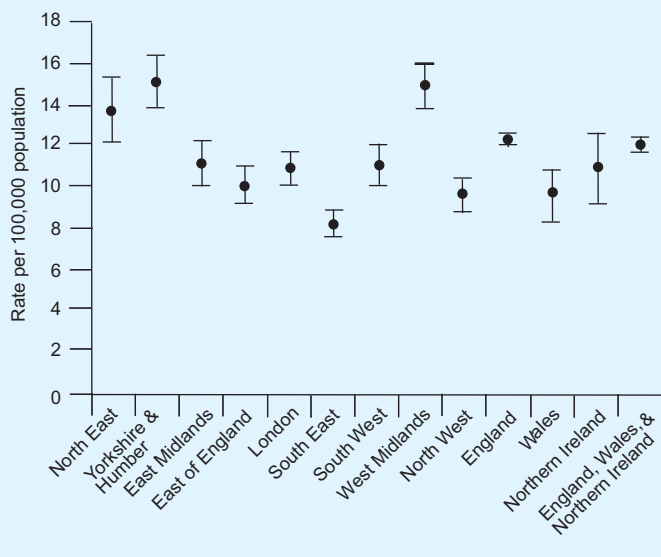
†Stata Statistical software: release 8.2. College Station, Texas, Stata Corporation, 2001.

Table 2 Laboratory and susceptibility ascertainment data for *Enterococcus* spp bacteraemia reports: England, Wales, and Northern Ireland: 2003

Region	Number of laboratories*	Number reporting <i>Enterococcus</i> spp bacteraemias (%)	Number reporting susceptibility information for <i>Enterococcus</i> spp bacteraemias† (%)
North East	11	10 (91)	10 (100)
Yorkshire & Humber	21	20 (95)	18 (90)
East Midlands	11	10 (91)	8 (80)
East of England	18	18 (100)	18 (100)
London	32	20 (63)	15 (75)
South East	29	22 (76)	21 (95)
South West	18	18 (100)	18 (100)
West Midlands	20	20 (100)	19 (95)
North West	31	22 (71)	21 (95)
England	191	160 (84)	148 (93)
Wales	14	12 (86)	10 (83)
Northern Ireland	12	10 (83)	6 (60)

*Provisional data. †As a proportion of those reporting bacteraemias.

Figure 1 Region-specific rates* of *Enterococcus* spp bacteraemia: England, Wales, and Northern Ireland: 2003



*Rates calculated using 2003 mid-year population estimates

Antibiotic susceptibility

Due to the low numbers of reports of the minor *Enterococcus* species, antibiotic susceptibilities were only analysed for the two most common species, *E. faecalis* and *E. faecium*.

For both *E. faecalis* and *E. faecium*, 21% of reports did not contain information on susceptibility to ampicillin/amoxycillin. There were 101 reports of *E. faecalis* isolates resistant to ampicillin/amoxycillin in 2003 (table 3), representing 5% of the total number of reports with susceptibility information. The proportion of resistant *E. faecalis* isolates varied geographically, from 10% in the London and Yorkshire and Humberside regions, to none in Northern Ireland. *E. faecium*, by contrast, is typically resistant to ampicillin/amoxycillin, although 16% (124 isolates) were reported as sensitive. The South East region had the lowest proportion of *E. faecium* isolates reported resistant to ampicillin/amoxycillin at 67%. All reports of *E. faecium* from Northern Ireland (that contained susceptibility results) indicated resistance.

Eighty-six per cent of reports of both *E. faecalis* and *E. faecium* did not include information on susceptibility to high-level gentamicin (resistance is indicated by a MIC >128 mg/L). Of the reports that did include this information, 38% of *E. faecalis* and 36% of *E. faecium* had high-level resistance to gentamicin (table 3). A further 20% *E. faecalis* and 24% *E. faecium* reports (521 and 24 respectively) indicated either resistance or sensitivity to gentamicin, but without specifying whether this was at high or low concentrations. Routine testing and reporting of high-level gentamicin susceptibility is encouraged, as enterococci have inherent low-level resistance to gentamicin. Nevertheless, serious enterococcal infections may be treated with combinations of cell wall active agents (ampicillin/amoxycillin or glycopeptides) and gentamicin, which show synergy in that the combination is bactericidal. High-level resistance to gentamicin, however, abolishes

Table 3 *Enterococcus* spp bacteraemia laboratory reports, England, Wales, and Northern Ireland: 2003

	Resistant (%) [*]	Sensitive	No Information (%) [†]
<i>E. faecalis</i> (n=2647)			
Ampicillin/amoxycillin	101 (5)	1984	562 (21)
Vancomycin	44 (2)	1815	788 (30)
Teicoplanin	38 (4)	999	1610 (61)
High level gentamicin	143 (38)	236	2268 (86)
Quinupristin/dalfopristin	173 (90)	19	2455 (93)
<i>E. faecium</i> (n=1011)			
Ampicillin/amoxycillin	675 (84)	124	212 (21)
Vancomycin	118 (16)	624	269 (27)
Teicoplanin	60 (14)	384	567 (56)
High level gentamicin	50 (36)	87	874 (86)
Quinupristin/dalfopristin	9 (8)	103	899 (89)

*As a percentage of reports with susceptibility information.

†As a percentage of all reports.

this synergy.

E. faecalis is inherently resistant to quinupristin/dalfopristin, and this may account for why 93% of reports of this species did not include susceptibility information for this antibiotic. Of the few reports that did include this information, 90% indicated resistance (table 3). A slightly higher proportion (11%) of *E. faecium* isolates contained susceptibility information for quinupristin/dalfopristin, of which 8% were resistant to this antibiotic.

GRE (Glycopeptide-resistant enterococci)

Seventy per cent of *E. faecalis* reports included information on susceptibility to vancomycin, and 73% of *E. faecium* reports contained this information (table 3). Fewer than half the reports for both *E. faecalis* and *E. faecium* contained data for teicoplanin (39% and 44% respectively). Seventy-four per cent of *E. faecalis* reports included susceptibility information for any glycopeptide, compared to 77% of reports of *E. faecium*.

Twenty-six per cent (698) of *E. faecalis*, did not contain information on the susceptibility of the isolate to either vancomycin or teicoplanin, and 36% (947) had information on susceptibility of the isolate to both glycopeptides (table 4). Thirty-four per cent of reports only included information on susceptibility to vancomycin, and 3% only contained information on teicoplanin.

The susceptibility reporting was similar for *E. faecium*; of the total number of reports, 40% included results for both glycopeptides, and 23% included results for neither (table 4). Thirty-three per cent of reports only had results for vancomycin, and 3% only contained results for teicoplanin.

Of the two main enterococcal species, higher proportions of glycopeptide resistance were seen among *E. faecium*, with 16% of reports indicating that the isolate was resistant to vancomycin, and 14%

Table 4 Glycopeptide susceptibility reporting for *E. faecalis* and *E. faecium* bacteraemia: England, Wales, and Northern Ireland: 2003

Susceptibility reported	<i>E. faecalis</i> (%)	<i>E. faecium</i> (%)
Vancomycin & teicoplanin	947 (36)	409 (40)
Neither vancomycin nor teicoplanin	698 (26)	234 (23)
Vancomycin only	912 (34)	333 (33)
Teicoplanin only	90 (3)	35 (3)

*Percentages do not add up to 100% due to rounding errors.

indicating resistance to teicoplanin (table 3). By comparison, 2% and 4% of *E. faecalis* reports indicated resistance to vancomycin and teicoplanin respectively.

The North East, and Yorkshire and Humberside regions did not report any *E. faecalis* isolates resistant to vancomycin, whereas the South West, and Wales both reported the highest percentage of vancomycin-resistant isolates (5%). Variation among the English regions in reported vancomycin resistance for *E. faecium* ranged from 0% in the North East to 27% in the East of England. Northern Ireland did not report any glycopeptide resistance in either *E. faecalis* or *E. faecium* in 2003, although at least half of the reports did not contain any information on glycopeptide susceptibility.

Age distribution

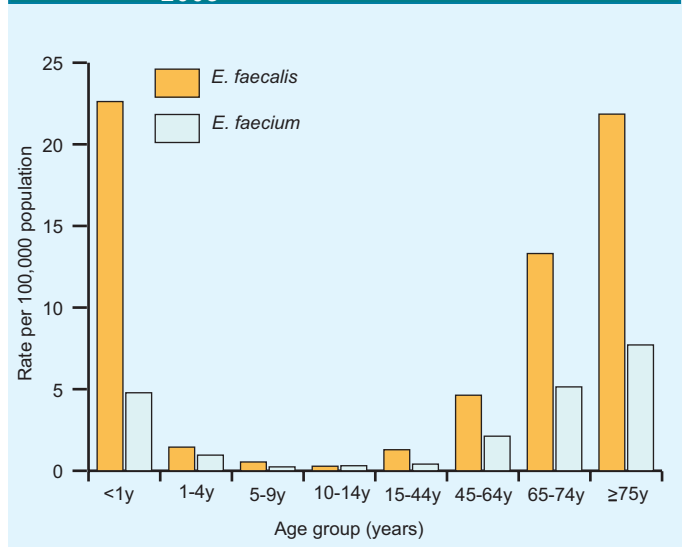
Patients with bacteraemia due to either *E. faecium* or *E. faecalis* show similar age distributions (figure 2), with the highest rates being in the very young (*ie*, those aged under one year) and the elderly (*ie*, those aged over 75 years and over).

Discussion

There was a 20% increase in the total number of enterococci reported in 2003 compared to 2002 (2). The number of reports of the two commonest species, *E. faecalis* and *E. faecium* increased by 25% and 24% respectively. There was a 17% decrease in the number of isolates reported as Group D streptococci. It is unlikely that speciation of group D streptococci accounts for much of the increase in the other enterococci, as *E. faecalis* increased from 2126 reports in 2002 to 2647 in 2003, and *E. faecium* from 816 to 1011, compared to a decrease from 259 to 216 reports of group D streptococci. It is more likely that this fall indicates the decline of disused nomenclature. The rate of enterococcal bacteraemia in England, Wales, and Northern Ireland increased from 9.4 per 100,000 population in 2002 to 11.9/100,000 in 2003.

An important issue with the enterococci is the technical problems associated with accurately identifying the species. The proportion of *Enterococcus* spp not identified further than the genus decreased marginally from 33% in 2002 to 32% in 2003. The recent report of the national glycopeptide-resistant enterococci (GRE) bacteraemia surveillance working group (3) recommended that all enterococci should be identified to species level. The recommendation was that identification should be based on the use of

Figure 2 Age-specific rates of *Enterococcus* spp bacteraemia per 100,000 population*, England, Wales, and Northern Ireland: 2003



* Based on mid-year 2003 population estimates.

commercial kits, while acknowledging that these are not always accurate, particularly for rarer species. Molecular techniques are more accurate, but are impractical and expensive for use in routine testing and are mostly used for reference purposes. As a result of this, misidentification occurs – some of which can be seen when examining the isolate’s antibiotic susceptibilities.

Currently in the United Kingdom, the vast majority of *E. faecalis* isolates are susceptible to ampicillin/amoxycillin, whereas *E. faecium* isolates are usually resistant. A crude analysis assuming that all *E. faecalis* are susceptible and all *E. faecium* are resistant, and based on the figures given above, would indicate that 5% of reported *E. faecalis* did not belong to that species, and 16% of *E. faecium* were also incorrectly identified. This represents a slight improvement in 2003 compared to 2002. The results of the 2001-2002 British Society for Antimicrobial Chemotherapy (BSAC) Bacteraemia Resistance Surveillance Programme (4), in which species identification was checked using reference techniques, found ampicillin resistance among *E. faecalis* isolates was 0.3%, and among *E. faecium* isolates was 86.2%. Comparing the BSAC results to those presented here, there is a suggestion that more *E. faecium* are being misidentified as *E. faecalis* than vice versa.

In contrast to the situation with ampicillin/amoxycillin, *E. faecalis* is inherently resistant to quinupristin/dalfopristin (although occasional susceptible isolates have been discovered and have been attributed to mutations knocking out a putative efflux pump) whereas *E. faecium* is inherently susceptible, although resistance can emerge. In 2003, 90% of *E. faecalis* and 8% of *E. faecium* were reported as resistant to this antibiotic, although the number of reports with information for this antibiotic is considerably lower than for ampicillin/amoxycillin. The report of the national working group(2) recommended that any apparent ampicillin/amoxycillin-resistant and/or

quinupristin/dalfopristin-sensitive *E. faecalis*, or ampicillin/amoxicillin-sensitive, and/or quinupristin/dalfopristin-resistant *E. faecium* should be sent to a reference laboratory for checking.

Between 2002 and 2003, the reporting of glycopeptide susceptibility improved slightly for both vancomycin and teicoplanin, and for both main enterococcal species. The proportion of reports identifying GRE has either remained stable or declined between the two years. For *E. faecalis* the percentage of isolates reported as resistant to vancomycin fell from 4% in 2002 to 2% in 2003, and teicoplanin resistance remained at 4%. Among *E. faecium* isolates, vancomycin resistance fell from 19% of isolates in 2002 to 16% in 2003, and the proportion reported as resistant to teicoplanin fell slightly from 14% to 13%.

The higher proportion of *E. faecalis* isolates resistant to teicoplanin compared to vancomycin is likely to be an artefact, possibly related to the high proportion of reports without information on teicoplanin susceptibility (61%), as there is no known genotype that confers resistance to teicoplanin, but not vancomycin. The two main genotypes conferring resistance to glycopeptides in *E. faecalis* and *E. faecium* are *vanA* (which confers resistance to both vancomycin and teicoplanin), and *vanB*, which confers resistance to vancomycin, but not teicoplanin. It is, therefore, expected that reported resistance to vancomycin should be slightly higher than resistance to teicoplanin in these two species, as seen for *E. faecium*. For the same reason, it is recommended that all laboratories should test vancomycin against enterococci, and that teicoplanin susceptibility, if tested, should only be tested in addition to vancomycin, even if it is the hospital's preferred glycopeptide for therapeutic purposes (3). Three per cent of reports of both *E. faecalis* and *E. faecium* in 2003 only contained information on teicoplanin susceptibility.

This pattern of slightly higher reported resistance to vancomycin compared to teicoplanin, and similar resistance rates to those reported here, were also seen in the BSAC Bacteraemia Resistance Surveillance Programme (4). For 2001-2002, the proportion of *E. faecalis* isolates reported as resistant to vancomycin and teicoplanin were 3.0% and 2.7% respectively. For *E. faecium*, the proportions resistant were 19.6% for vancomycin and 15.2% for teicoplanin. The 95% confidence intervals for these percentages overlap the percentage resistances reported through the Health Protection Agency's voluntary reporting system. This

suggests that despite the known problems associated with species identification, this system provides a reasonably accurate estimate of the proportion of enterococcal bacteraemias that are resistant to the glycopeptides.

Mandatory surveillance of GRE (5) along the lines of that already in place for methicillin-resistant *Staphylococcus aureus* (MRSA), commenced in October 2003 and it is expected that the first results will be published in 2005. It will be interesting to discover the extent to which the voluntary reporting scheme underestimates the level of GRE in England and whether, allowing for this, it still provides a reasonably accurate estimate of the proportion of antibiotic-resistant pathogens, as has been seen for *S. aureus*/MRSA.

Acknowledgements

These reports would not be possible without the enduring weekly contributions from microbiology colleagues in laboratories across England, Wales, and Northern Ireland, without which there would be no surveillance data.

Please send any comments/feedback to Andrew Pearson, email andrew.pearson@hpa.org.uk or Louise Bishop, email louise.bishop@hpa.org.uk. In addition, the support from colleagues within the Health Protection Agency is valued in the preparation of this report. These contributions are greatly appreciated.

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