

Voluntary surveillance of *Enterococcus* spp bacteraemia, England, Wales, and Northern Ireland: 2004

Key points:

- In 2004 there were 6314 voluntary reports of *Enterococcus* spp bacteraemia, compared to 6285 reports in 2003.
- Mandatory surveillance of glycopeptide resistant enterococci (GRE) bacteraemia commenced in October 2003. The results for the first year of this scheme will be published by the Department of Health.
- *Enterococcus faecalis* accounted for 63% and *Enterococcus faecium* 28% of reports identified to species level, although examination of reported resistance patterns, particularly ampicillin/amoxycillin and dalbopristin/quinupristin, has highlighted possible misidentification of enterococci.
- More than half of the *E. faecalis* and *E. faecium* reports were in those aged 65 years and over.
- Susceptibility reporting indicated that 2% of *E. faecalis* bacteria and 22% of *E. faecium* bacteria were resistant to vancomycin.
- Unexpectedly, resistance to linezolid was reported in five out of 842 enterococci reports. Linezolid resistance is exceptional and any such isolates should be forwarded to the Health Protection Agency's Antibiotic Resistance Monitoring and Reference Laboratory (ARMRL). Investigation of unusual resistance reports is a function of this reference service.

Introduction

This report describes *Enterococcus* spp (including Group D streptococci) isolated from specimens in 2004 by laboratories in England, Wales, and Northern Ireland and voluntarily reported to the Health Protection Agency Centre for Infections. Age- and region-specific rates were calculated using Office for National Statistics

2003 mid-year population estimates. Where the percentage resistance to a specific antibiotic is given, the denominator excludes those reports without any susceptibility information for that antibiotic. Confidence intervals were calculated using the STATA* commercial statistical package.

In 2004 there were 6314 reports (table 1) of

Table 1 Laboratory reports* of *Enterococcus* spp bacteraemia: England, Wales, and Northern Ireland: 2003-2004

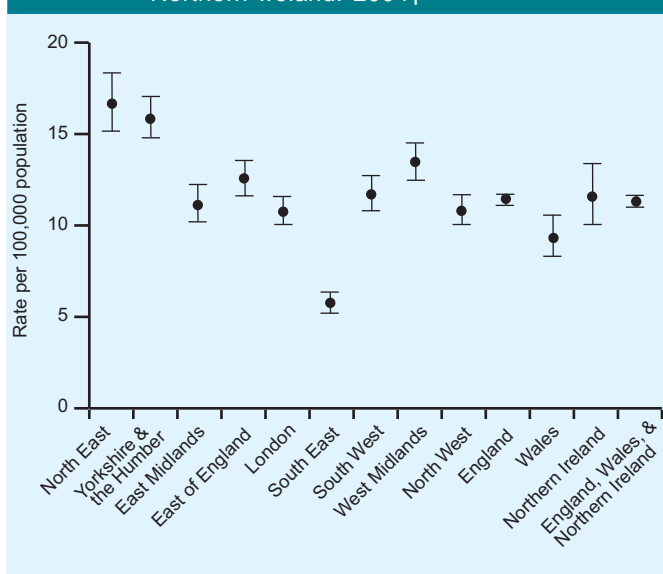
| <i>Enterococcus</i> spp | Number of reports 2004 (%)† | Number of reports 2003 (%)† |
|--|-----------------------------|-----------------------------|
| <i>Enterococcus</i> not fully identified | 1902 | 2011 |
| <i>E. avium</i> | 57 (1) | 39 (1) |
| <i>E. casseliflavus</i> | 28 (1) | 21 (0.5) |
| <i>E. durans</i> | 52 (1) | 51 (1) |
| <i>E. faecalis</i> | 2794 (63) | 2767 (65) |
| <i>E. faecium</i> | 1225 (28) | 1069 (25) |
| <i>E. gallinarum</i> | 101 (2) | 96 (2) |
| <i>E. hirae</i> | 3 (0.1) | 4 (0.1) |
| <i>E. raffinosus</i> | 3 (0.1) | 5 (0.1) |
| Streptococci group D | 149 (3) | 222 (5) |
| Total | 6314 | 6285 |

*Provisional data.

†As a percentage of reports identified to species level.

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

Figure 1 Region-specific rates* of *Enterococcus* spp bacteraemia: England, Wales, and Northern Ireland: 2004†



*Rates calculated using 2003 mid-year population estimates.

†Provisional data.

Table 2 Laboratory and susceptibility ascertainment data* for *Enterococcus* spp bacteraemia reports: England, Wales, and Northern Ireland: 2004

| Region | Number of bacteraemia reporting 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 | 22 | 20 (91) | 19 (95) |
| East Midlands | 11 | 11 (100) | 9 (82) |
| East of England | 19 | 19 (100) | 19 (100) |
| London | 31 | 19 (61) | 19 (100) |
| South East | 27 | 20 (74) | 19 (95) |
| South West | 18 | 18 (100) | 18 (100) |
| West Midlands | 20 | 19 (95) | 19 (100) |
| North West | 31 | 21 (68) | 20 (95) |
| England | 190 | 157 (83) | 152 (97) |
| Wales | 14 | 11 (79) | 9 (82) |
| Northern Ireland | 12 | 11 (92) | 7 (64) |

*Provisional data.

†As a proportion of those reporting bacteraemias.

‡As a proportion of those reporting *Enterococcus* spp bacteraemias.**Table 3** *Enterococcus* spp bacteraemia laboratory reports, England, Wales, and Northern Ireland: 2003-2004†

| 2004 | Resistant | | Sensitive | | No Information | | 2003 | Resistant | | Sensitive | | No Information | |
|------------------------------------|-----------|------|-----------|------|----------------|------------------------------------|----------|-----------|------|-----------|--|----------------|--|
| | (%)* | | (%) | | (%) | | | (%)* | | (%) | | (%) | |
| <i>E. faecalis</i> (n=2794) | | | | | | <i>E. faecalis</i> (n=2767) | | | | | | | |
| Ampicillin/amoxycillin | 88 (4) | 2149 | 557 | (20) | | Ampicillin/amoxycillin | 110 (5) | 2030 | 627 | (23) | | | |
| Vancomycin | 46 (2) | 1966 | 782 | (28) | | Vancomycin | 58 (3) | 1858 | 851 | (31) | | | |
| Teicoplanin | 39 (3) | 1250 | 1505 | (54) | | Teicoplanin | 51 (5) | 1020 | 1696 | (61) | | | |
| High level gentamicin | 159 (41) | 230 | 2405 | (86) | | High level gentamicin | 156 (39) | 243 | 2368 | (86) | | | |
| Dalfopristin/quinupristin | 252 (89) | 30 | 2512 | (90) | | Dalfopristin/quinupristin | 174 (90) | 19 | 2574 | (93) | | | |
| <i>E. faecium</i> (n=1225) | | | | | | <i>E. faecium</i> (n=1069) | | | | | | | |
| Ampicillin/amoxycillin | 840 (87) | 125 | 260 | (21) | | Ampicillin/amoxycillin | 710 (85) | 125 | 245 | (23) | | | |
| Vancomycin | 199 (22) | 718 | 308 | (25) | | Vancomycin | 128 (17) | 644 | 299 | (28) | | | |
| Teicoplanin | 108 (18) | 497 | 620 | (51) | | Teicoplanin | 67 (15) | 394 | 610 | (57) | | | |
| High level gentamicin | 41 (23) | 136 | 1048 | (86) | | High level gentamicin | 52 (36) | 91 | 926 | (87) | | | |
| Dalfopristin/quinupristin | 8 (4) | 177 | 1040 | (85) | | Dalfopristin/quinupristin | 10 (9) | 105 | 954 | (89) | | | |

*As a percentage of reports with susceptibility information.

†Provisional data.

Enterococcus spp bacteraemia (including Group D streptococci). *E. faecalis* accounted for 63% and *E. faecium* accounted for 28% of the reports identified to species level. Of the 216 laboratories in England, Wales, and Northern Ireland, 179 (83%) reported at least one *Enterococcus* spp bacteraemia in 2004 (table 2). Of the 179 laboratories, 168 (94%) included some susceptibility information for enterococci.

The reporting rate for *Enterococcus* spp bacteraemia for England, Wales, and Northern Ireland combined was 11.6 per 100,000 population (figure 1).

Antibiotic susceptibility

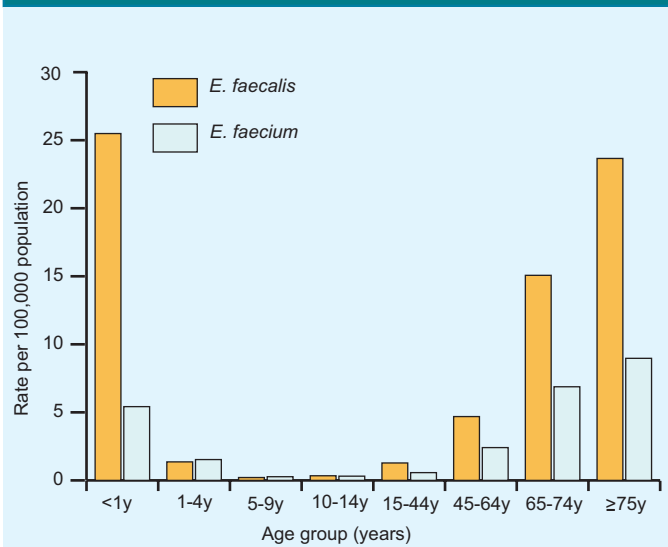
Due to the low numbers of reports of the minor *Enterococcus* species (and validity of identification), antibiotic susceptibilities were only analysed for the

two major species; *E. faecalis* and *E. faecium*.

E. faecalis is typically susceptible to ampicillin/amoxycillin. Eighty-eight reports of *E. faecalis* isolates resistant to ampicillin/amoxycillin were made in 2004, representing only 4% of the total number of reports with this susceptibility information (table 3). Previously, *E. faecalis* reports were more 'contaminated' with *E. faecium*s in which vancomycin resistance is more common. The lower error rate in identification may account for apparent shifts in the percentage vancomycin resistance seen in *E. faecalis* reports. *E. faecalis* is inherently resistant to quinupristin/dalfopristin. Of the few reports that did include this information, 89% indicated resistance (table 3).

In contrast, *E. faecium* is generally resistant to ampicillin/amoxycillin and sensitive to dalfopristin/quinupristin. Thirteen per cent (125) of isolates with a

Figure 2 Age-specific rates of *Enterococcus* spp bacteraemia per 100,000 population*, England, Wales, and Northern Ireland: 2004†



*Rates calculated using 2003 mid-year resident population estimates.
†Provisional data.

susceptibility result for ampicillin/amoxycillin were reported as sensitive.

Fifteen per cent of *E. faecium* isolates contained susceptibility information for dalfopristin/quinupristin, of which 4% were resistant.

Unexpectedly, resistance to linezolid was reported in five of 842 enterococci tested. It is recommended that any samples that appear to be resistant to linezolid should be sent to the Health Protection Agency's Antibiotic Resistance Monitoring and Reference Laboratory (ARMRL), 61 Colindale Avenue, London, NW9 5HT, (tel: 020 8327 6511) to provide a reference source for confirmation and investigation.

GRE (Glycopeptide-resistant enterococci)

Seventy-two per cent of *E. faecalis* reports included information on susceptibility to vancomycin, and 75% of *E. faecium* reports contained this information (table 3).

Of the two major enterococcal species, higher proportions of glycopeptide resistance were seen among *E. faecium*, with 22% of reports indicating that the isolate was resistant to vancomycin, and 18% indicating resistance to teicoplanin (table 3). By comparison, 2% and 3% of *E. faecalis* reports indicated resistance to vancomycin and teicoplanin respectively.

Twenty-six reports indicated resistance to teicoplanin and susceptibility to vancomycin. These reports came from 19 laboratories, at least one in every region except for Northern Ireland where no teicoplanin resistance was reported. These reports have not been independently confirmed.

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 65 years

and over).

Ascertainment

Ascertainment in 2004 was assessed by calculating the number of laboratories that reported *Enterococcus* spp as a percentage of the number of laboratories reporting any bacteraemias for each region (table 2). Regional ascertainment scores using this method ranged from 61% to 100%. For some regions, low rates of *Enterococcus* spp bacteraemia can be attributed in part to low ascertainment scores.

Discussion

There was a 0.5% increase in the total number of *Enterococcus* spp bacteraemia reported in the voluntary surveillance scheme in 2004 compared to 2003 (1). The number of reports of the two commonest species, *E. faecalis* and *E. faecium* increased by 1% and 15% respectively, but their relative proportions as a percentage of reports identified to species level remained similar (63% and 28% respectively). There was a 33% fall in the number of isolates reported as Group D streptococci. It is likely that this fall indicates the decline of disused nomenclature, as well as improved laboratory practice confirming the identification of *Enterococcus* spp. Speciation of group D streptococci would not account for much of the increase in the other enterococci, since the number of group D streptococci reduced by only 73 reports, while the increase in the number of reports between 2003 and 2004 for *E. faecium*, for example, was 156.

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 level decreased marginally from 32% in 2003 to 30% in 2004. The report of the National GRE Bacteraemia Surveillance Working Group in 2004 (2) recommended that all enterococci should be identified to species level. Misidentification may still occur due to delays in adjusting to these recent recommendations as well as limitations of the identification kits that are currently available.

The results of the 2001-2002 British Society for Antimicrobial Chemotherapy (BSAC) Bacteraemia Resistance Surveillance Programme (3), in which species identification was confirmed using molecular techniques, found ampicillin resistance among *E. faecalis* isolates was 0.3%, and among *E. faecium* isolates was 86.2%. In the 2004 voluntary data, as shown in table 3, ampicillin/amoxycillin resistance was 4% and 87% for *E. faecalis* and *E. faecium* isolates respectively. These data suggest that some *E. faecium* may have been incorrectly identified as *E. faecalis*.

In contrast to the situation with ampicillin/amoxycillin, *E. faecalis* is inherently resistant to dalfopristin/quinupristin (although occasional susceptible isolates have been discovered) whereas *E. faecium* is inherently susceptible, although resistance can emerge. In 2004, 89% of *E. faecalis* and 4% 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). These results further support the suggestion that some misidentification of species has occurred.

The report of the National GRE Bacteraemia Surveillance Working Group (2) recommended that any apparent ampicillin-resistant/amoxycillin and/or dalfopristin/quinupristin-sensitive *E. faecalis*, or ampicillin/amoxycillin-sensitive and/or dalfopristin/quinupristin-resistant *E. faecium*, as well as any isolates resistant to both agents, should be sent to ARMRL for investigation.

For *E. faecalis*, the percentage of isolates reported as resistant to vancomycin decreased from 3% to 2% between 2003 and 2004. Among *E. faecium* isolates, vancomycin resistance rose from 17% of isolates in 2003 to 22% in 2004. These values are similar to those reported by the BSAC Bacteraemia Resistance Surveillance Programme, which reported vancomycin resistance in *E. faecalis* as 3% and in *E. faecium* as 19.6% (3). This suggests that despite the known problems associated with species identification, this system provides a reasonably accurate estimate of the proportion of enterococci that are resistant to the glycopeptides.

Since all known glycopeptide resistance genotypes confer resistance to vancomycin (4), 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 (2). Four per cent of reports of both *E. faecalis* and *E. faecium* in 2003 contained information on teicoplanin susceptibility alone. Resistance to teicoplanin but not vancomycin is not a pattern of resistance that has previously been confirmed. There is no known genotype that confers resistance to teicoplanin but not vancomycin. It is recommended that any such isolates be forwarded to ARMRL at Colindale for investigation.

Eighty-six per cent of reports for 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, 41% of *E. faecalis* and 23% of *E. faecium* had high-level resistance to gentamicin (table 3). A further 701 *E. faecalis* and 313 *E. faecium* reports (25% and 26% respectively) indicated either resistance or sensitivity to gentamicin, but without specifying whether this was at high or low levels. Routine testing and reporting of high-level gentamicin susceptibility is encouraged, as enterococci have inherent low-level gentamicin resistance. Nonetheless, gentamicin potentiates cell wall active agents (ampicillin/amoxycillin or glycopeptides) to produce a bactericidal effect so long as resistance is only low-level. This synergy is abolished if bacteria acquire high-level resistance to gentamicin.

The method for assessing ascertainment employed here (table 2) can only give an approximate indication of the standard of reporting. Comparisons between a region's *Enterococcus* spp bacteraemia rate and its ascertainment score should therefore be made with

caution. Ascertainment was assessed by calculating the number of laboratories that reported *Enterococcus* spp as a percentage of the number of laboratories reporting any bacteraemias for each region. A region's ascertainment may therefore be overestimated if it has laboratories that report some but not all of the enterococci detected. The method also assumes that all laboratories would encounter bacteraemias due to enterococci at some point during the year. Ascertainment may be underestimated if a region contains laboratories, which deal with small numbers of samples where it is plausible that they have not encountered any enterococci. Additionally, some smaller laboratories may have protocols to forward certain specimens to larger laboratories for testing. If these specimens are then reported by the larger laboratories it may look as if the smaller laboratories have not received any enterococci thus underestimating a region's ascertainment.

Mandatory surveillance of GRE (5) similar to that already in place for methicillin resistant *Staphylococcus aureus* (MRSA), commenced in October 2003. It will be interesting to compare results from the two schemes.

Acknowledgements

These reports would not be possible without the weekly contributions from microbiology colleagues in laboratories across England, Wales, and Northern Ireland, without whom there would be no surveillance data. The support from colleagues within the Health Protection Agency, Specialist and Reference Microbiology Division, in particular, is valued in the preparation of the reports. Feedback is welcome, and should be addressed to either Andrew Pearson (email: andrew.pearson@hpa.org.uk), Allison Lee (email: allison.lee@hpa.org.uk), or Karen Wagner (email: karen.wagner@hpa.org.uk).

Reference List

1. Health Protection Agency. *Enterococcus* spp bacteraemia: England, Wales, and Northern Ireland, 2003. *Commun Dis Rep CDR Wkly* [serial online] 18 November 2004 [cited 12 March 2005]; **14** (47): Bacteraemia. Available at: <http://www.hpa.org.uk/cdr/archives/2004/cdr4704.pdf>.
2. Health Protection Agency. National Glycopeptide-Resistant Enterococcal Bacteraemia Surveillance Working Group. Report to the Department of Health. London: HPA, 2004. <http://www.hpa.org.uk/infections/publications/pdf/GRE%20bact%20surveillance%20final%20Aug04.pdf>.
3. Reynolds R, Potz N, Colman M, Williams A, Livermore D, MacGowan A. Antimicrobial susceptibility of the pathogens of bacteraemia in the UK and Ireland 2001-2002: the BSAC Bacteraemia Resistance Surveillance Programme. *J Antimicrob Chemother* 2004; **53**:1018-1032.
4. French G L. Enterococci and Vancomycin Resistance. *Clinical Infect Dis*. 1998; **27**(Suppl 1): S75-83.
5. HPA. Surveillance of glycopeptide resistant enterococcal bacteraemias. *Commun Dis Rep CDR Wkly* [serial online] 2003 [cited 11 March 2005]; **13**(29): News. Available at: <http://www.hpa.org.uk/cdr/archives/2003/cdr2903.pdf>.