

Proteus spp, *Morganella morganii*, and *Providencia* spp bacteraemias, England, Wales, and Northern Ireland: 2003

Key points:

- There was a 14% increase in *Proteus mirabilis* bacteraemia reports made via the voluntary reporting scheme in England, Wales, and Northern Ireland in 2003 compared with reports in 2002. During the same time period, the number of reports of *Morganella morganii* increased by 16%.
- Seventy-seven per cent of the *P. mirabilis* bacteraemia reports made in 2003 were accompanied by susceptibility information for one or more antibiotics.
- The majority (69.7%) of *M. morganii* bacteraemia reports included susceptibility information to one or more antibiotics.
- Four *P. mirabilis* isolates were reported resistant to all the antimicrobials listed in table 2 of this report.
- For both *Proteus* species and *M. morganii* bacteraemia reports, rates of infection were highest among the 75 years and over age group, and the rates of both these bacteraemias per 100,000 population were more than double in females.

This report covers bacteraemias due to *Proteus* species, *Morganella morganii*, and *Providencia* species reported by laboratories in England, Wales, and Northern Ireland in 2003. All laboratory reports described here concern isolation of these species from blood culture with or without cerebrospinal fluid. Rates are calculated using Office for National Statistics (ONS) 2002 mid-year resident population denominators for each corresponding age and regional boundary.

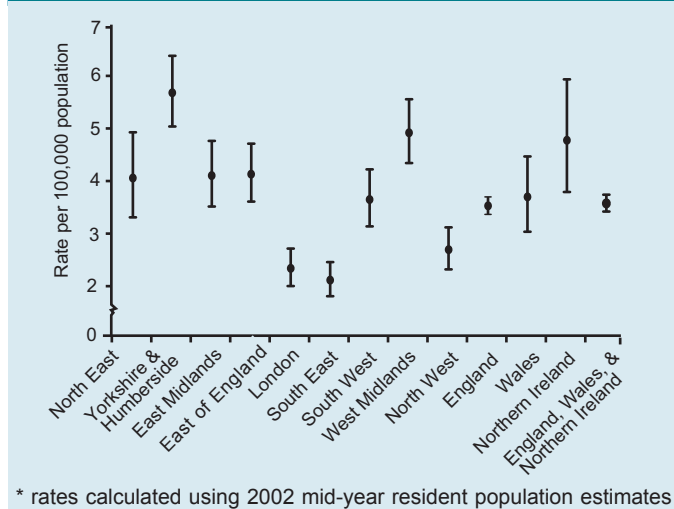
Recent outbreaks of *E. coli* producing CTX-M Extended-spectrum β -lactamases (ESBLs) have been found in a number of regions in England, with some of these infections resulting in bacteraemias (1). It is unclear whether these infections are hospital or community-acquired. Questionnaires have been sent to regional leads/regional epidemiologists to establish the extent of current investigations and the extent of any data ascertainment issues. *E. coli* reports for 2003 have therefore not been included in this report, but will be reported later in the year following further investigation and analysis.

Regional distributions

Proteus spp bacteraemia

There were 1937 provisional reports received of *Proteus* species bacteraemia from England, Wales, and Northern Ireland in 2003 (table 1 and figure 1). As in 2002, *P. mirabilis* accounted for the majority of *Proteus* reports (80%; 1542). Of the other *Proteus* species, the most commonly reported were *P. vulgaris* (5%; 87) and *P. penneri* (0.1%; 2), 0.3% were identified as other named *Proteus* species. Sixteen per cent of *Proteus* reports (301) were not identified beyond the genus level. The highest rates of *Proteus* bacteraemia reports were from Yorkshire and Humberside (5.7 per 100,000) and the West Midlands (4.9/100,000 population). The lowest

Figure 1 Region-specific rates of bacteraemia due to *Proteus* spp: England, Wales, Northern Ireland:



reporting rates were from the South East (2.1/100,000), and London (2.3/100,000). The overall *Proteus* bacteraemia reporting rate was 3.5/100 000 in England, 3.7/100,000 for Wales, and 4.8/100,000 for Northern Ireland.

Morganella morganii bacteraemia

Three hundred and ninety-three bacteraemia reports for *Morganella morganii* were received in 2003 (table 1 and figure 2). Within England, Yorkshire and Humberside had the highest reporting rate (1.1 per 100,000 population) followed by the North East (0.95/100,000) and West Midlands regions (0.94/100,000). The lowest reporting rate was from the South West (0.42/100,000). The overall *M. morganii* bacteraemia reporting rate for England was

Table 1 Antibiotic susceptibilities for *Morganella morganii*, *Proteus* spp bacteraemia laboratory reports Wales, and Northern Ireland: 2003

	North East	Yorkshire & Humberside	East Midlands	Eastern of England	London	South East	South West	West Midlands	North West	England	Wales	Northern Ireland	E,W,&NI*
<i>Morganella morganii</i>	24	55	27	37	44	49	21	50	42	349	36	8	393
<i>Proteus mirabilis</i>	89	217	122	171	142	151	143	216	155	1406	59	77	1542
<i>Proteus penneri</i>	–	–	–	–	–	–	1	–	–	1	1	–	2
<i>Proteus vulgaris</i>	2	14	6	15	18	5	5	12	5	82	2	3	87
<i>Proteus</i> spp	9	52	45	35	12	14	32	33	22	254	46	1	301
Other named	2	–	–	3	–	–	–	–	–	5	–	–	5
<i>Proteus</i> spp	–	–	–	–	–	–	–	1	1	2	–	–	2
<i>Providencia alcalifaciens</i>	–	3	–	2	2	2	2	2	1	14	–	1	15
<i>Providencia rettgeri</i>	1	12	3	3	5	5	4	8	4	45	2	4	51
<i>Providencia stuartii</i>	–	–	1	6	–	1	1	2	1	12	1	–	13

*E,W, & NI = England, Wales, and Northern Ireland

0.70/100,000. Wales and Northern Ireland had reporting rates for *M. morganii* of 1.23 and 0.47/100,000 respectively.

Providencia species bacteraemia

Eighty-three bacteraemias were reported as being caused by *Providencia* species in 2003, the majority of which were due to *Providencia stuartii* (61%; 51) (table 1). Owing to the small number of reports, no further analyses were performed on these data.

Antimicrobial resistance patterns

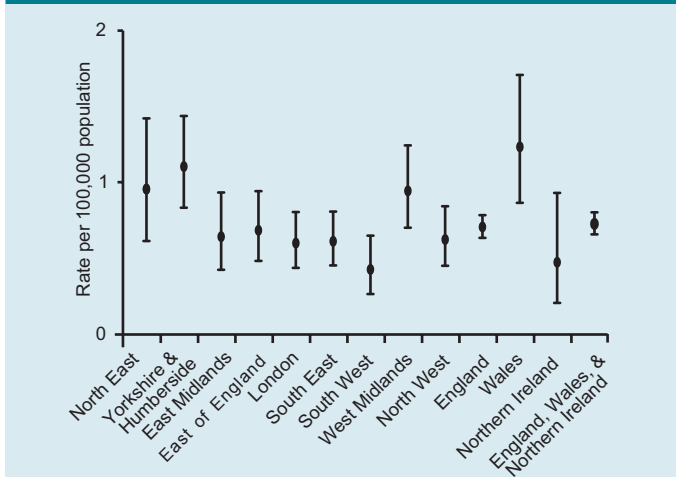
Proteus spp bacteraemia

Seventy-seven per cent (1182/1542) of the *Proteus mirabilis* bacteraemia reports made in 2003 were accompanied by susceptibility information for one or more of the

antibiotics listed in table 2. The most widely reported antimicrobial was gentamicin (1105) followed by amoxycillin/ampicillin (1053), cefuroxime (1012), ciprofloxacin (997), ceftazidime (685), and cefotaxime (437).

Reporting of amoxycillin/ampicillin susceptibilities in *P. mirabilis* bacteraemia isolates ranged from 46.2% in South West region to 88.9% in East of England. Seventy-three per cent of *P. mirabilis* reports made from Wales contained information on amoxycillin/ampicillin resistance compared with 45.5% of reports from Northern Ireland and 69.3% from England. Amoxycillin/ampicillin resistance in *Proteus mirabilis* was most commonly reported by London (39.4%), and was least common in reports from the North East (23.9%). Amoxycillin/ampicillin resistance was indicated

Figure 2 Region-specific rates of bacteraemia due to *Morganella morganii*: England, Wales, and Northern Ireland: =2003



* rates calculated using 2002 mid-year resident population estimates

Figure 3 Ampicillin/amoxycillin susceptibility data for *Proteus mirabilis* reported from bacteraemias, England, Wales, and Northern Ireland: 2003

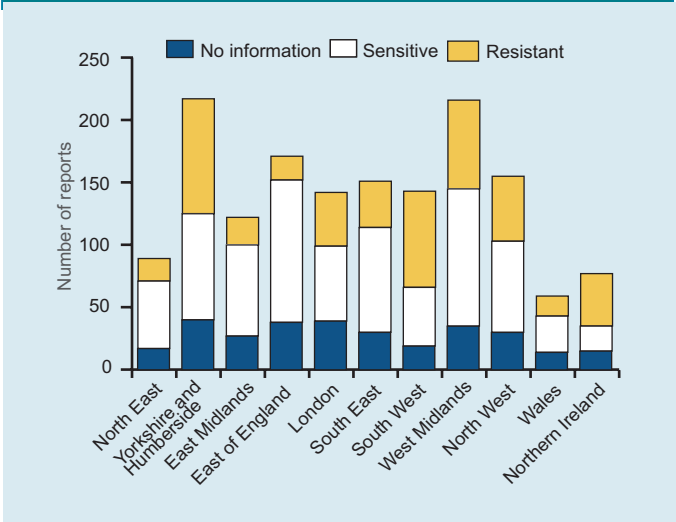


Table 2 Antibiotic susceptibilities for *Morganella morganii*, *Proteus* spp bacteraemia laboratory reports, England, Wales, and Northern Ireland: 2003

	Sensitive	Resistant (%) [*]	No information (%) [†]
<i>Proteus mirabilis</i> (n=1542)			
Amoxicillin/ampicillin	749	304 (29)	489 (32)
Cefuroxime	994	18 (2)	530 (34)
Cefotaxime	429	8 (2)	1105 (72)
Ceftazidime	1542	48 (3)	48 (3)
Ciprofloxacin	949	42 (4)	551 (36)
Gentamicin	1063	7 (1)	472 (31)
<i>Proteus vulgaris</i> (n=87)			
Ciprofloxacin	55	2 (4)	30 (34)
Cefotaxime	25	1 (4)	61 (70)
Ceftazidime	42	– (–)	45 (52)
Gentamicin	60	1 (2)	26 (30)
Imipenem	18	1 (5)	68 (78)
<i>Morganella morganii</i> (n=393)			
Ciprofloxacin	247	18 (7)	128 (33)
Cefotaxime	113	20 (15)	260 (66)
Ceftazidime	169	22 (12)	202 (51)
Gentamicin	252	22 (8)	119 (30)
Imipenem	92	11 (11)	290 (74)
<i>Providencia stuartii</i> (n=51)			
Amikacin	10	– (–)	41 (80)
Ciprofloxacin	30	2 (6)	19 (37)
Cefotaxime	17	– (–)	34 (67)
Ceftazidime	23	– (–)	28 (55)
Imipenem	10	– (–)	41 (80)

* As a percentage of reports with susceptibility information.

† As a percentage of total reports.

in 32.6% and 42.9% in *Proteus mirabilis* reported from Wales and Northern Ireland, respectively (figure 3).

The proportion of amoxicillin/ampicillin resistant *P. mirabilis* isolates (304) that were also resistant to cefuroxime (15/264), cefotaxime (8/129), ceftazidime (7/192), ciprofloxacin (32/265) and gentamicin (13/190) was 6%, 6%, 4%, 12%, and 7% respectively (table 4). This compares with resistance to cefuroxime (1/644), cefotaxime (0/278) ceftazidime (0/472), ciprofloxacin (12/640) and gentamicin (23/713) of 0.2%, 0%, 0%, 1.9%, and 3.2% respectively for ampicillin/amoxicillin-sensitive isolates, indicating an association between ampicillin/amoxicillin resistance and resistance to other antimicrobials (table 3).

There were only 18 reports of cefuroxime resistance

(1.8%; 18/1012) in England and Wales, eight reports of cefotaxime resistance (1.9%; 8/437) and seven reports of ceftazidime resistance (3.7%; 7/191) in *Proteus mirabilis* bacteraemia isolates reported from England, Wales, and Northern Ireland in 2003 (figures 4-6).

Ciprofloxacin resistance in *P. mirabilis* ranged from 1.5% in the North East to 15.7% in London (figure 7). Wales reported no isolates with resistance to ciprofloxacin, while Northern Ireland reported just three isolates (11.1% of isolates with ciprofloxacin susceptibility data). Of the 48 reports indicating ciprofloxacin resistance, 72.7%, 11.1%, 17.4%, 14.7%, and 22.9% were amoxicillin/ampicillin (32/44), cefuroxime (5/45), cefotaxime (4/23), ceftazidime (5/34), and gentamicin (8/35) resistant respectively (table 3).

Of the 1105 *P. mirabilis* bacteraemia reports with gentamicin susceptibility information, 42 indicated gentamicin resistance (3.8%). Gentamicin resistance varied from no reports from the North East to 8.3% of reports in the West Midlands. None of the reports with gentamicin susceptibility information from Northern Ireland (0/34) indicated resistance (figure 8). Of the 42 gentamicin-resistant isolates 13/36 were resistant to amoxicillin/ampicillin, 5/37 were resistant to cefuroxime, 5/11 were resistant to cefotaxime, 4/30 were ceftazidime, and 8/44 were resistant to ciprofloxacin (table 3).

Of the *P. mirabilis* bacteraemia reports made in 2003, with antimicrobial susceptibility results, four isolates were reported with resistance to all antimicrobials tested (table 3).

As there were only small numbers of reports of *P. vulgaris* and *P. penneri*, regional breakdowns and multiple resistance patterns were not examined. *P. vulgaris* and *P. penneri* are inherently resistant to ampicillin and cefuroxime.

The majority of *Morganella morganii* bacteraemia reports included susceptibility information to one or more of the antibiotics listed in table 2 (69.7%). The same percentage of *M. morganii* reports contained susceptibility data for gentamicin, of which 8% reported resistance to this antimicrobial, a 3% increase in gentamicin resistance compared with reports in 2002. Resistance to cefotaxime was reported in 15% of reports with susceptibility information for this antimicrobial. Ceftazidime resistance was reported in 12% of reports, 7% of *M. morganii* reports (with susceptibility results for ciprofloxacin reported resistance to the antimicrobial), and 8% of reports with susceptibility data were resistant to gentamicin. Eleven per cent of reports with susceptibility data for imipenem reported resistance to this antimicrobial. This is a substantial increase on 2002, when only 6% resistance was reported for imipenem (table 2). *M. morganii* is inherently resistant to ampicillin.

There were 51 *Providencia stuartii* bacteraemia reports in 2003 (table 2) of which 35 included susceptibility information for ciprofloxacin, cefotaxime, ceftazidime, and imipenem. Ciprofloxacin resistance was indicated in two of the 35 reports (5.7%). No antibiotic resistance was reported other than ampicillin and gentamicin. *P. stuartii* is inherently resistant to these two antimicrobials.

Table 3 Multiple antibiotic resistance patterns shown in laboratory reports for *Proteus mirabilis* bacteraemia, England, Wales, and Northern Ireland: 2003

	Amoxycillin/ ampicillin		Cefuroxime		Cefotaxime		Ceftazidime		Ciprofloxacin		Gentamicin	
	Resistance (n=304)	Sensitive (n=749)	Resistance (n=18)	Sensitive (n=994)	Resistance (n=8)	Sensitive (n=429)	Resistance (n=7)	Sensitive (n=678)	Resistance (n=48)	Sensitive (n=949)	Resistance (n=42)	Sensitive (n=1063)
Amoxycillin/ ampicillin												
Resistant (%)			15 (94)	249 (28)	8 (100)	121 (30)	7 (100)	185 (28)	32 (73)	233 (27)	13 (36)	277 (29)
Sensitive			1	643	–	278	–	472	12	628	23	690
No Information			2	102	–	30	–	22	4	88	6	96
Cefuroxime												
Resistant (%)	15 (6)	1 (–)			7 (100)	4 (1)	6 (100)	8 (1)	5 (11)	10 (1)	5 (14)	13 (1)
Sensitive	249	643			–	370	–	618	40	815	32	906
No Information	40	105			1	55	1	52	3	124	5	144
Cefotaxime												
Resistant (%)	8 (6)	– (–)	7 (64)	– (–)			6 (100)	1 (–)	4 (17)	4 (1)	5 (45)	3 (1)
Sensitive	121	278	4	370			–	338	19	389	6	411
No Information	175	471	7	624			1	339	25	556	31	649
Ceftazidime												
Resistant (%)	7 (4)	– (–)	6 (43)	– (–)	6 (86)	– (–)			5 (15)	2 (–)	4 (13)	3 (–)
Sensitive	185	472	8	618	1	338			29	621	26	644
No Information	112	277	4	376	1	91			14	326	12	416
Ciprofloxacin												
Resistant (%)	32 (12)	12 (2)	5 (33)	40 (5)	4 (50)	19 (5)	5 (71)	29 (4)			8 (18)	27 (3)
Sensitive	233	628	10	815	4	389	2	621			36	881
No Information	39	109	3	139	–	21	–	28			2	155
Gentamicin												
Resistant (%)	13 (4)	23 (3)	5 (28)	32 (3)	5 (63)	6 (1)	4 (57)	26 (4)	8 (23)	36 (4)		
Sensitive	277	690	13	906	3	411	3	644	27	881		
No Information	14	36	–	56	–	12	–	8	13	32		
Multiple Resistance[†]												
(%)	(1)		(44)		(67)		(80)		(24)		(50)	
Resistant	4/293		4/9		4/6		4/5		4/17		4/8	

* as a percentage of reports with susceptibility information

† resistant to amoxycillin/ampicillin, cefuroxime, cefotaxime/ ceftazidime, ciprofloxacin and gentamicin

As there were only small numbers of *M. morganii*, and *Providencia* species; regional breakdowns and multiple resistance patterns were not examined.

Age distributions

Proteus species bacteraemia reports were highest among the 75 years and over age group (figure 9); the rate of *Proteus* spp bacteraemias reported in males (41.8 per

100,000) was more than double the rate in females (17.1/100,000). The next highest age-specific rate was in the 65 to 74 years age group, which showed a similar gender distribution (11.6/100,000 in males and 4.5/100,000 in females).

Age-specific bacteraemia rates for *M. morganii* again showed a substantial difference between male and female rates in the over 45 year age groups. The

Figure 4 Cefuroxime susceptibility data for *Proteus mirabilis* reported from bacteraemias, England, Wales, and Northern Ireland: 2003

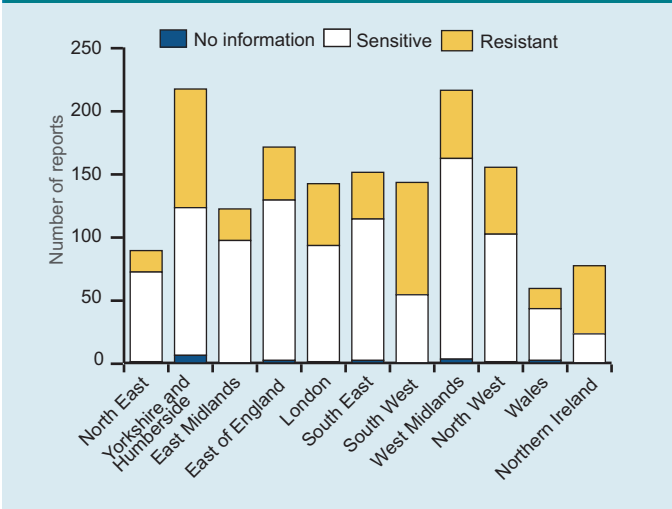


Figure 5 Cefotaxime susceptibility data for *Proteus mirabilis* reported from bacteraemias, England, Wales, and Northern Ireland: 2003

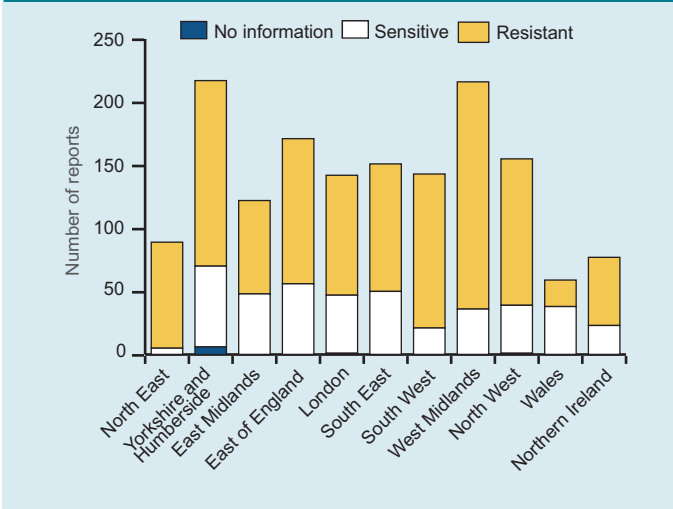


Figure 6 Ceftazidime susceptibility data for *Proteus mirabilis* reported from bacteraemias, England, Wales, and Northern Ireland: 2003

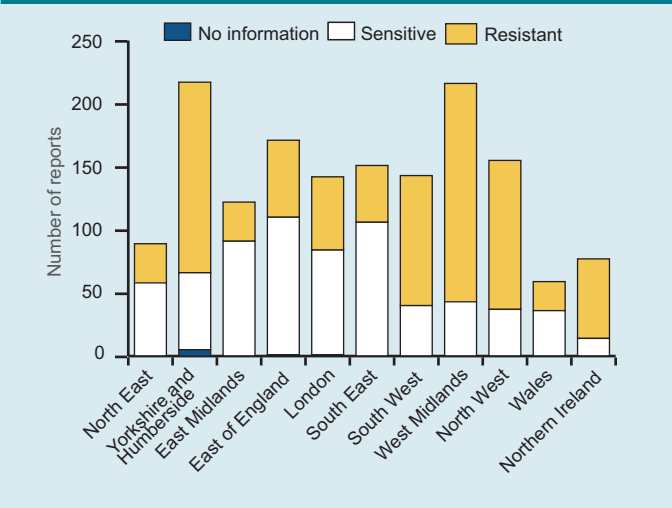
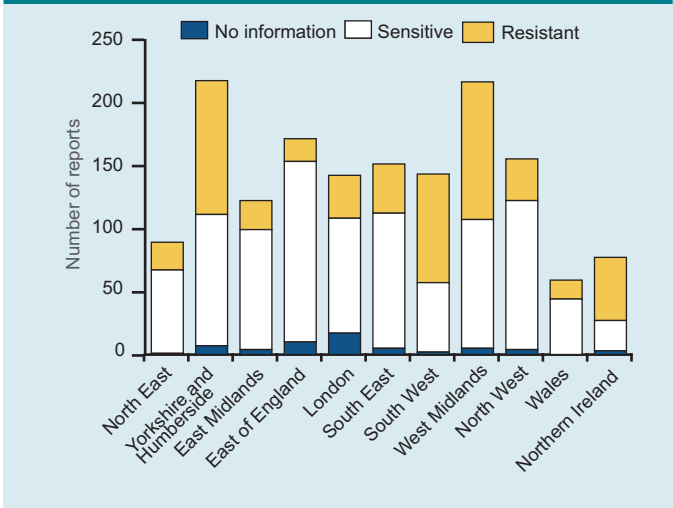


Figure 7 Ciprofloxacin susceptibility data for *Proteus mirabilis* reported from bacteraemias, England, Wales, and Northern Ireland: 2003



75 years and over age group reported the highest rates with a rate of bacteraemia in males double that in females (7.8/100,000 males and 3.26/100,000 females).

Discussion

Proteus mirabilis was the eighth leading cause of bacteraemia in England, Wales, and Northern Ireland in 2003, and the tenth leading cause in 2002. Of the Gram-negative bacteria, *P. mirabilis* was the fifth most common cause of bacteraemia in England, Wales, and Northern Ireland (2,3).

Bacteraemia laboratory reports for infections due to *Proteus* species and *Morganella morganii* have increased from 1501 reports in 1999 to 2330 in 2004, so far, an increase of approximately 55% (2-6).

Sixteen per cent of *Proteus* reports (301) were not identified beyond the genus level, which is unfortunate as *Proteus* species differ greatly in their antibiotic susceptibilities.

Figure 8 Gentamicin susceptibility data for *Proteus mirabilis* reported from bacteraemias, England, Wales, and Northern Ireland: 2003

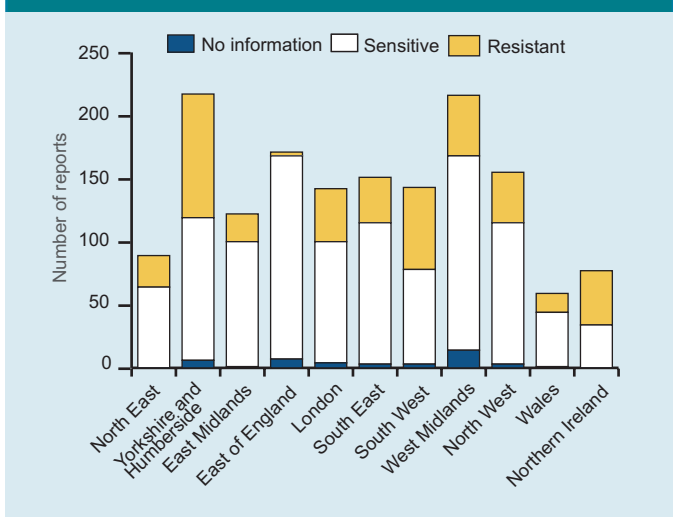
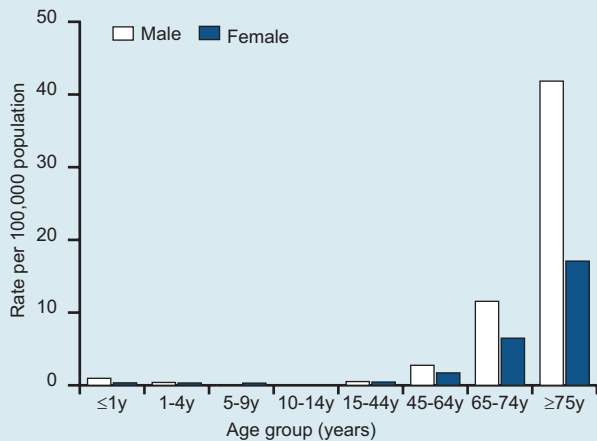
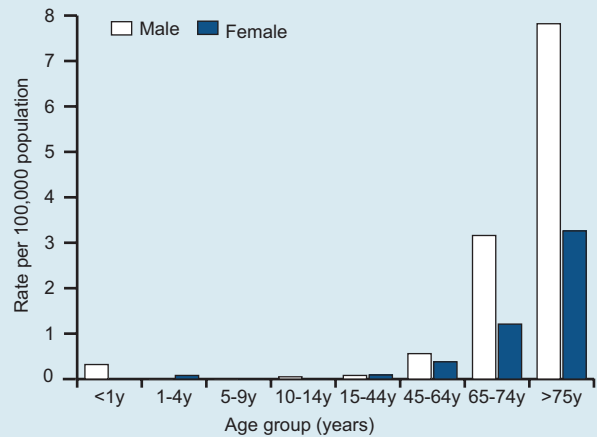


Figure 9 Age-specific rates of *Proteus* sp bacteraemia reports: England, Wales, and Northern Ireland:



* rates calculated using 2002 mid-year resident population

Figure 10 Age-specific rates of *Morganella morganii* spp bacteraemia reports: England, Wales, and Northern Ireland: 2003*



* rates calculated using 2002 mid-year resident population

There has been a small increase in the proportion of *P. mirabilis* isolates reported with amoxicillin/ampicillin resistance in 2003, but it would appear that the proportion of amoxicillin/ampicillin-resistant reports has stabilised at approximately 30%, between 2001 and 2003 (4,6). Eleven per cent of reports with susceptibility data for imipenem reported resistance to this antimicrobial. This is a substantial increase on 2002, when only 6% resistance was reported for imipenem (table 2). Of the Enterobacteriaceae, however, Proteaceae are the least susceptible to imipenem, and it is not uncommon to identify isolates with borderline resistance. The Health Protection Agency's Antibiotic Resistance Monitoring and Reference Laboratory does not seek submission of such isolates, but would be happy to look at any *Proteus* or *Morganella* isolates that appear to be resistant to meropenem (which is inherently more active against these genera than imipenem), or appear highly resistant to imipenem with an MIC >8mg/L by ETest, or growing up to a standard 10µg disc.

Differences in the reporting of antimicrobial susceptibilities between regions may account for the variation in resistance seen. It is not possible to confirm whether the increases seen in bacteraemias, due to the species reported here or the increases in antimicrobial resistance, are due to enhanced ascertainment of data (reporting of cases), or whether they reflect a real increase in the number of bacteraemias and a real increase in the levels of antimicrobial resistance. Similarly, it is not possible to determine the cause of variation in levels of reported antimicrobial resistance between regions. Indeed, the data reported here are considered provisional as the Health Protection Agency's Communicable Disease Surveillance Centre continues to receive 2003 bacteraemia reports from regions.

Acknowledgements

These reports would not be possible without the weekly contributions from microbiology colleagues in laboratories across England, Wales, and Northern Ireland,

without which there would be no surveillance data. Feedback is welcome, and should be addressed to either Andrew Pearson (email: <andrew.pearson@hpa.org.uk> or Allison Lee <alison.lee@hpa.org.uk>. In addition, the support from colleagues within the Health Protection Agency, Specialist and Reference Microbiology Unit, in particular, is valued in the preparation of the reports.

References

1. HPA. Infections with organisms carrying extended-spectrum β-lactamases in the community: first report. *Commun Dis Rep CDR Wkly* [serial online] 2003 [cited 19 February 2004];13(32):Bacteraemia. Available at <<http://www.hpa.org.uk/cdr/PDFfiles/2003/cdr0332.pdf>>.
2. HPA. Bacteraemia, England, Wales and Northern Ireland: laboratory reports 2002 and 2003. *Commun Dis Rep CDR Wkly* [serial online] 2004 [cited 19 February 2004];14(3):Bacteraemia. Available at <<http://www.hpa.org.uk/cdr/PDFfiles/2004/cdr0304.pdf>>.
3. PHLS. Bacteraemia, England and Wales: laboratory reports 2001 and 2002. *Commun Dis Rep CDR Wkly* [serial online] 2003 [cited 19 February 2004]; 13(3): Bacteraemia. Available at <<http://www.hpa.org.uk/cdr/PDFfiles/2003/cdr0303.pdf>>.
4. PHLS. *Escherichia coli*, *Proteus* spp., *Morganella morganii* and *Providencia* spp bacteraemias: England and Wales, 2001. *Commun Dis Rep CDR Wkly* [serial online] 2002 [cited 19 February 2004];12 (8): Bacteraemia. Available at <<http://www.hpa.org.uk/cdr/PDFfiles/2002/cdr0802.pdf>>.
5. PHLS. Group A, C and G streptococci; *Escherichia coli*; and *Proteus* spp. *Morganella morganii* bacteraemia, England and Wales: January to December 2000. *Commun Dis Rep CDR Wkly* [serial online] 2001 [cited 19 February 2004]; 11(11): Bacteraemia. Available at <<http://www.hpa.org.uk/cdr/PDFfiles/2001/cdr1101.pdf>>.
6. PHLS. *Escherichia coli*, *Proteus* spp., *Morganella morganii* and *Providencia* spp bacteraemias: England, Wales and Northern Ireland: 2002. *Commun Dis Rep CDR Wkly* [serial online] 2002 [cited 19 February 2004]; 13 (8): Bacteraemia. Available at <<http://www.hpa.org.uk/cdr/PDFfiles/2003/cdr0803.pdf>>.