when the MIC of carbapenems for the infecting organism is >4 μg/mL. Since the optimal treatment for these infections is not known and the therapeutic options are limited, it is critical to implement effective antibiotic policies and strict infection control measures in order to limit their dissemination.

References

[1] Jacoby GA, Munoz-Price LS. The new beta-lactamases. N Engl J Med 2005;352:380–91.
[2] Rossolini GM. Acquired metallo-beta-lactamases: an increasing clinical threat. Clin Infect Dis 2005;41:1557–8.
[3] Walsh TR, Toleman MA, Poirel L, Nordmann P. Metallo-beta-lactamases: the quiet before the storm? Clin Microbiol Rev 2005;18:306–25.
[4] Cornaglia G, Mazzariol A, Lauretti L, Rossolini GM, Fontana R. Hospital outbreak of carbapenem-resistant *Pseudomonas aeruginosa* producing VIM-1, a novel transferable metallo-beta-lactamase. Clin Infect Dis 2000;31:1119–25.
[5] Giakkoupi P, Xanthaki A, Kanelopoulou M, et al. VIM-1 metallo-beta-lactamase-producing *Klebsiella pneumoniae* strains in Greek hospitals. J Clin Microbiol 2003;41:3893–6.
[6] Luzzaro F, Docquier JD, Colinon C, et al. Emergence in *Klebsiella pneumoniae* and *Enterobacter cloacae* clinical isolates of the VIM-4 metallo-beta-lactamase encoded by a conjugative plasmid. Antimicrob Agents Chemother 2004;48:648–50.
[7] Tenover FC, Arbeit RD, Goering RV, et al. Interpreting chromosomal DNA restriction patterns produced by pulsed-field gel electrophoresis: criteria for bacterial strain typing. J Clin Microbiol 1995;33:2233–9.
[8] Knaus WA, Draper EA, Wagner DP, Zimmerman JE. APACHE II: a severity of disease classification system. Crit Care Med 1985;13:818–29.

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In vitro susceptibility of Spanish isolates of *Neisseria gonorrhoeae* to cefditoren and five other antimicrobial agents

Sir,

Gonococcal resistance is an increasing problem for gonorrhoea treatment, since *Neisseria gonorrhoeae* is adept at developing resistance mechanisms to new agents. Early *N. gonorrhoeae* were extremely susceptible to antimicrobials, but since the 1950s strains resistant to several antibiotics have been described. Chromosomally mediated, low-level penicillin and tetracycline resistance as well as β-lactamase-mediated high-level penicillin resistance were described more than 30 years ago. Currently, the more remarkable trends in antimicrobial resistance are related to quinolones, with the emergence of isolates with intermediate or full resistance [1], and the maintenance in Spain of full susceptibility to spectinomycin and third-generation parenteral cephalosporins [2]. Therefore, there is a continuous need for information on antimicrobial susceptibility patterns, including susceptibility testing of antibiotics with potential use in gonorrhoea treatment such as third-generation oral cephalosporins.

A total of 204 selected clinical isolates of *N. gonorrhoeae* (15 serogroup IA and 189 serogroup IB isolates; 78.9% strains were β-lactamase negative) received at the reference laboratory during 2004 and 2005 were tested by agar dilution method following Clinical and Laboratory Standards Institute (CLSI) recommendations [3]. Inocula were prepared on supplemented GC agar plates and the growth was suspended in Mueller–Hinton broth to an optical density of 0.5 McFarland standard (10^5 colony-forming units (CFU)/mL). An inoculator device dispensed a final inoculum of 10^4 CFU/spot on GC agar. Incubation was performed in a 5% CO_2 atmosphere at 37 °C for 18–20 h. *Neisseria gonorrhoeae* 6395 (β-lactamase positive) and *N. gonorrhoeae* 3303 (penicillin resistant and β-lactamase negative) were used as controls; interexperiment variations with these strains were not more than ±1 dilution. Current CLSI breakpoints were considered [4].

Table 1 shows the in vitro activity of the antimicrobials, with the third-generation cephalosporins ceftriaxone and cefditoren showing the highest intrinsic activity based on minimum inhibitory concentration for 90% of the organisms (MIC_{90}) (0.007 μg/mL and 0.12 μg/mL, respectively). By applying the CLSI breakpoint for susceptibility for ceftriaxone (≤0.25 μg/mL) to cefditoren, 100% susceptibility to

Table 1
Minimum inhibitory concentrations (MICs) and percentage of susceptible (S), intermediate (I) and resistant (R) strains according to Clinical and Laboratory Standard Institute (CLSI) breakpoints

Antimicrobial	MIC (μg/mL)			%S	%I	%R
	MIC_{50}	MIC_{90}	Range			
Penicillin	1	128	≤0.007 to >128	10	59	31
Cefoxitin	1	4	0.12–4	87	13	0
Cefditoren	0.015	0.12	≤0.007–0.25	–[a]	–[a]	–[a]
Ceftriaxone	≤0.007	0.007	≤0.007–0.12	100	0	0
Ciprofloxacin	0.06	16	≤0.007–32	50	7	43
Tetracycline	1	8	0.06–32	15	49	36

[a] CLSI breakpoint not available.

cefditoren is obtained, similar to ceftriaxone.

The non-susceptibility pattern of strains used in this study was similar to that for the year 2005 for penicillin non-susceptibility (87.1% vs. 90% in this study), but was higher for ciprofloxacin non-susceptibility (39.3% vs. 50% in this study). If we compare results obtained previously in our laboratory in the period 1992–1999 [5] and in 2001 [2] with those from all the strains received during 2005, cefoxitin non-susceptibility (intermediate + resistant) rates increased from 5.2% (in 1992–1999) to 12.3% (in 2001) and 10% (in 2005), and ciprofloxacin non-susceptibility rates increased from 6.5% to 12.3% and 39.3%, respectively. Non-susceptibility rates were in the range of 76–90% for penicillin and 64–87% for tetracycline, with 100% susceptibility to ceftriaxone.

Japan has reported a decrease in susceptibility to cephems, very slightly affecting cefditoren and ceftriaxone [6]. The use of cefixime or other oral cephems (ceftibuten, cefpodoxime) with reduced affinity for mosaic penicillin-binding protein 2 (PBP2) may have selected this type of resistant strain [7], whilst ceftriaxone and cefditoren, owing to the long side chain at the C3 cephem position, possess strong affinity for the altered PBP2 resulting in very slight reduction in activity [7].

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References

[1] Alcalá B, Arreaza L, Salcedo C, et al. Molecular characterization of ciprofloxacin resistance of gonococcal strains in Spain. Sex Transm Dis 2003;30:395–8.
[2] Arreaza L, Salcedo C, Alcalá B, Berrón S, Martín E, Vázquez JA. Antibiotic resistance of *Neisseria gonorrhoeae* in Spain: trends over the last two decades. J Antimicrob Chemother 2003;51:153–6.
[3] National Committee for Clinical Laboratory Standards. Methods for dilution antimicrobial susceptibility tests for bacteria that growth aerobically. Approved standard M7-A6. Wayne, PA: NCCLS; 2003.
[4] Clinical and Laboratory Standards Institute. Performance standards for antimicrobial susceptibility testing. Fifteenth informational supplement M100-S15. Wayne, PA: CLSI; 2005.
[5] Berrón S, Vazquez JA, Giménez MJ, de la Fuente L, Aguilar L. In vitro susceptibilities of 400 Spanish isolates of *Neisseria gonorrhoeae* to gemifloxacin and 11 other antimicrobial agents. Antimicrob Agents Chemother 2000;44:2543–4.
[6] Tanaka M, Nakayama H, Tunoe H, et al. A remarkable reduction in the susceptibility of *Neisseria gonorrhoeae* isolates to cephems and the selection of antibiotic regimens for the single-dose treatment of gonococcal infection in Japan. J Infect Chemother 2002;8:81–6.
[7] Takahata S, Senju N, Osaki Y, Yoshida T, Ida T. Amino acid substitutions of mosaic penicillin-binding protein 2 associated with reduced susceptibility to cefixime in clinical isolates of *Neisseria gonorrhoeae*. Antimicrob Agents Chemother 2006;50:3638–45.

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In vitro antimicrobial activity of *N*-acetylcysteine against bacteria colonising central venous catheters

Sir,

It is estimated that ca. 5% of the 5 million central venous catheters (CVCs) that are inserted in critically ill patients each year in the USA result in bloodstream infections [1]. These 250 000 episodes of catheter-related bloodstream infections prolong hospital stay and result in substantial morbidity and