diagnostic tests and access to guidelines for common diseases of childhood.

Our study has several implications for public health policy and research. Although in all countries cultural factors may influence antibiotic prescribing practices, their level of influence appears to be less in Switzerland. When developing programmes for judicious use of antibiotics in relatively low-consumption countries, specific attention should focus on other factors such as improved diagnostic tests and development and distribution of guideline. Our results are likely to apply to other central and north European countries with low antibiotic use.

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In vitro activity of cefditoren against clinical isolates of *Escherichia coli* from a Korean hospital

Sir,

The emergence of fluoroquinolone resistance in *Escherichia coli* is of great concern because fluoroquinolones are critically important for treating serious infections caused by *E. coli* in humans [1]. Although fluoroquinolones have been successfully used for the treatment of *E. coli* infections, recently a significant increase in fluoroquinolone resistance among *E. coli* isolates has been reported [2]. Thus, alternatives should be considered as treatment options for *E. coli* infections. Cefditoren, formerly ME-1206, is a methoxyimino cephalosporin utilised clinically as a pivoxil ester, which enhances oral absorption [3]. Although increasing trends of antimicrobial resistance in *E. coli* isolates require the use of alternative treatment options, the in vitro activity of cefditoren against *E. coli* isolates has not yet been evaluated in Korea. Given the high prevalence of antimicrobial resistance in Korea, evaluation of the antimicrobial activity of cefditoren against *E. coli* to determine antimicrobial resistance is warranted.

A total of 307 non-duplicate clinical isolates of *E. coli*, collected from a tertiary care hospital in Korea (Samsung Medical Center, Seoul) in 2005, were investigated: 267 (87.0%) were from urine and 40 (13.0%) were from blood. In vitro susceptibility testing was performed for cefditoren and seven other comparator agents: ciprofloxacin, amoxicillin/clavulanic acid, gentamicin, trimethoprim/sulfamethoxazole, cefazolin, ceftriaxone and cefixime. Susceptibility testing was performed using the broth microdilution method according to the guidelines of the Clinical and Laboratory Standards Institute (CLSI) [4]. Interpretive criteria for susceptibility were those recommended by the CLSI [4]. Quality control was performed using *Staphylococcus aureus* ATCC 29213, *Enterococcus faecalis* ATCC 29212, *Pseudomonas aeruginosa* ATCC 27853, *E. coli* ATCC 25922, *E. coli* ATCC 35218 and *Klebsiella pneumoniae* ATCC 700603. Extended-spectrum β-lactamase (ESBL) production was detected by the clavulanic acid double-disk synergy method using a BBL Sensi-Disc Antimicrobial Susceptibility TEST Disc (Becton, Dickinson and Company, Sparks, MD). The χ^2-test and Fisher's exact test were used to determine the significance of differences in resistance rates where appropriate. Mann–Whitney *U*-test was used to compare the mean rank of minimum inhibitory concentration (MIC) values for cefditoren because no interpretative criteria for cefditoren have been published.

Table 1 summarises the in vitro susceptibilities for the eight antimicrobial agents, including cefditoren, against 307 *E. coli* isolates from urine or blood. The results show that ceftriaxone and cefixime had high susceptibility rates for *E. coli* isolates (90.9% and 84.4%, respectively). These two drugs also showed low MIC_{50} and MIC_{90} values (MIC for 50% and 90% of the organisms, respectively). Owing to the lack of a resistance breakpoint for cefditoren, it was not pos-

Table 1
Antimicrobial susceptibility among 307 *Escherichia coli* isolates

Antimicrobial agent	MIC (mg/L)			Susceptibility[a]		
	Range	MIC_{50}	MIC_{90}	*%S*	*%I*	*%R*
Cefditoren	≤0.0625 to >64	0.25	16	–[b]	–[b]	–[b]
Cefazolin	1 to >64	4	>64	67.1	11.1	21.8
Ceftriaxone	≤0.0625 to >64	0.125	2	90.9	0.3	8.8
Cefixime	≤0.0625 to >64	0.5	8	84.4	4.6	11.0
Amoxicillin/clavulanic acid	1/0.5 to 64/32	16/8	32/16	35.2	32.6	32.2
Gentamicin	0.5 to >64	4	>64	66.8	10.4	22.8
Ciprofloxacin	≤0.03125 to >32	0.0625	>32	68.4	1.3	30.3
Trimethoprim/sulfamethoxazole	≤0.0625/1.1875 to >64/1216	0.5/9.5	>64/1216	57.0	0	43.0

MIC, minimum inhibitory concentration; $MIC_{50/90}$, MIC for 50% and 90% of the organisms, respectively.
[a] Percent susceptible (*%S*), percent intermediate (*%I*) and percent resistant (*%R*) according to the interpretive criteria of the Clinical and Laboratory Standards Institute [4].
[b] No interpretative breakpoint for cefditoren has been published.

sible to evaluate its resistance rate. Nevertheless, we were able to compare the MIC_{50} and MIC_{90} of cefditoren with the other antimicrobial agents. MIC_{50} and MIC_{90} values of cefditoren for all *E. coli* isolates were 0.25 μg/mL and 16 μg/mL, respectively. The MIC_{50} of cefditoren was higher than those of ceftriaxone and ciprofloxacin, but lower than those of the others including cefixime. More than 30% of the *E. coli* isolates were non-susceptible to ciprofloxacin. ESBL production was detected in 24 *E. coli* isolates (7.8%), of which only 4 isolates (16.7%) were susceptible to ciprofloxacin and all were resistant to cefditoren.

Antimicrobial resistance was compared between *E. coli* isolates from blood and urine. Although the susceptibility rates in *E. coli* isolates from urine were lower than those from blood for most antimicrobial agents except cefazolin and amoxicillin/clavulanic acid, these differences were not significant ($P > 0.05$) (data not shown). Although MIC values of cefditoren were not significantly different between the two groups ($P = 0.517$), the MIC_{90} for isolates from blood (1 μg/mL) was much lower than that for isolates from urine (16 μg/mL). Such high MIC_{90} values in isolates from urine were also observed for ceftriaxone and cefixime (data not shown). As expected, the susceptibility rates of all antimicrobial agents tested were significantly lower in ciprofloxacin-resistant *E. coli* isolates than in ciprofloxacin-susceptible *E. coli* isolates ($P < 0.001$). Cefditoren showed good in vitro activity against ciprofloxacin-susceptible *E. coli* isolates. MIC_{50} and MIC_{90} values of cefditoren for ciprofloxacin-susceptible *E. coli* (0.25 μg/mL and 0.5 μg/mL, respectively) were lower than the other agents except ceftriaxone (data not shown).

Korea is one of the regions with the highest resistance rates (15–34%) to ciprofloxacin [5–7]. The results of this study confirmed reduced activity (resistance rate of 30.3%) of ciprofloxacin against *E. coli* isolates in Korea. This finding suggests probable limitation of the use of fluoroquinolones for the treatment of *E. coli* infections as a first-line choice. In addition, increasing use of ciprofloxacin against ciprofloxacin-susceptible isolates will increase ciprofloxacin resistance rates further. Thus, other antimicrobial agents should be considered as therapeutic options for the treatment of *E. coli* infections in Korea, not only to avoid treatment failure associated with ciprofloxacin resistance but also to reduce the usage amount of ciprofloxacin.

In this study, we evaluated the in vitro susceptibility of cefditoren against *E. coli* isolates obtained from urine or blood. As shown, cefditoren showed good in vitro activity against *E. coli*, especially against ciprofloxacin-susceptible isolates. Thus, cefditoren can be an alternative option for ciprofloxacin-susceptible *E. coli* isolates and its use would reduce the consumption of ciprofloxacin. Furthermore, cefditoren had moderate in vitro activity against ciprofloxacin-resistant strains.

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