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ANTIMICROBIAL SUSCEPTIBILITY

Natural antibiotic susceptibility of *Providencia stuartii, P. rettgeri, P. alcalifaciens* and *P. rustigianii* strains

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The natural antibiotic susceptibility of 38 *Providencia rettgeri*, 35 *P. stuartii*, 23 *P. alcalifaciens* and 20 *P. rustigianii* strains was examined. MIC values were determined by a microdilution procedure and evaluated by a table calculation programme. *P. stuartii* was the least susceptible *Providencia* sp. and was naturally resistant to tetracyclines, some penicillins, older cephalosporins, sulphamethoxazole and fosfomycin and to antibiotics to which other species of Enterobacteriaceae are also resistant. It was naturally sensitive to modern penicillins and cephalosporins, carbapenems and aztreonam, but its susceptibility to aminoglycosides and quinolones was difficult to assess. *P. alcalifaciens* and *P. rustigianii* strains were the most susceptible *Providencia* spp. They were naturally sensitive or intermediate to tetracyclines and sensitive to aminoglycosides and quinolones. Susceptibility to sparfloxacin, biapenem and sulphamethoxazole permitted the discrimination of *P. alcalifaciens* and *P. rustigianii* strains. The natural antibiotic susceptibility of *P. rettgeri* strains was between that of *P. stuartii* and that of the other providenciae. *P. rettgeri* was resistant to tetracyclines and fosfomycin, but more susceptible to aminoglycosides, quinolones, fosfomycin and numerous β-lactam antibiotics than *P stuartii*. A database is described of the natural antibiotic susceptibilities of *Providencia* spp. It can be used for the validation of antibiotic susceptibility test results of these micro-organisms.

Introduction

Providencia spp. are typical aetiological agents of nosocomial infections and are now of significant medical interest. This is attributed to the increase in numbers of elderly patients and improvements in medical care, resulting in a higher incidence of immunocompromised patients and increasing numbers of nosocomial infections.

From a medical point of view, *P. stuartii* is the most important species of the genus. *P. stuartii* has been identified frequently as a cause of nosocomial urinary tract infection (UTI). Predisposing circumstances like catheterisation and intubation favour the establishment of UTIs with this bacterium. Less frequently it also causes respiratory and skin infections and is isolated occasionally from surgical wounds. *P. stuartii* is a genomically homogeneous species and is found predominantly in the urine [1] and in the groin areas of hospitalised patients, but also in water samples [2].

P. rettgeri is also an important infectious agent of the human urinary tract, but is isolated less frequently than *P. stuartii*. In part this is because of the susceptibility of *P. rettgeri* to the aminoglycosides often used in the treatment of UTIs (and to which *P. stuartii* is less susceptible). *P. rettgeri* has been isolated from poultry, the faeces of reptiles and amphibians and from surface waters and, therefore, seems to be widely distributed in nature. There is evidence that *P. rettgeri* is also a pathogen for a wide range of animals. Recently, meningitis in crocodiles due to *P. rettgeri* has been documented [3].

In contrast to these species, which generally do not contribute to gastrointestinal infections of man, certain strains of *P. alcalifaciens* are invasive enteric pathogens that can cause diarrhoea [4, 5] including travellers' diarrhoea [6]. The species consists of two genospecies [7]. In 1983, a fourth species, *P. rustigianii* was

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described for strains that had previously been called *P. alcalifaciens* biovar 3 [8, 9]. *P. rustigianii* can be isolated from human faeces and can colonise the human intestinal tract, but its medical significance awaits further study. The *Providencia* sp. described most recently is *P. heimbachae* [10]. There is no evidence to date that this bacterium is of significance to man, because all isolates have been from penguin faeces and an aborted bovine fetus [11].

Many *Providencia* isolates, in particular *P. stuartii* strains, are resistant to numerous antibiotics. With the exception of *P. stuartii*, knowledge about the antibiotic susceptibility of *Providencia* spp. is relatively incomplete. This is partly because many laboratories identify providenciae only to the genus level and susceptibility testing is documented with only a few antibiotics. *P. stuartii* is the most resistant species of the genus and is generally considered to be an antibiotic multiresistant bacterium [1]. Like most other strains of the Proteeae, *P. stuartii* is resistant to polymyxin B, colistin and nitrofurantoin. The species is considered to be resistant also to some aminoglycosides and penicillins, older cephalosporins, tetracyclines and chloramphenicol. *P. rettgeri* and *P. alcalifaciens* strains are 'less resistant' than *P. stuartii* to aminoglycosides, cephalosporins and substituted penicillins [1, 11]. Cornaglia and co-workers found no significant differences in antibiotic susceptibility between *P. rettgeri* and *P. alcalifaciens* strains [12]. Otherwise, multiresistant *P. rettgeri* strains have been described [13, 14] and are not rare. The increasing significance of infections with *Providencia* spp. necessitates a more detailed elucidation of differences in antibiotic susceptibility between *Providencia* spp.

The object of this study was to establish a database for the natural susceptibility to a wide range of antibiotics of all *Providencia* spp. pathogenic to man. The data from 116 *Providencia* strains tested with 71 antibiotics can be valuable for the validation of routine susceptibility test results.

Materials and methods

Bacterial strains

A total of 116 *Providencia* strains was examined. The strains were clinical isolates from the culture collection of H. Grimm (Weingarten, Germany) and B. Vocht (Moers, Germany) and from our culture collection. The latter originated from a multicentre study of the Paul Ehrlich Society conducted in 1986 with 30 centres in Germany, Switzerland and Austria and from the collection of MERLIN-Diagnostika (Bornheim, Germany). The majority of the strains submitted by H. Grimm, B. Vocht and MERLIN were recent isolates and were collected between 1990 and 1997. Copy strains (more than the isolate/patient) and duplicate strains from the same outbreak were excluded.

Identification

All strains were identified to the species level with a commercial identification system for Enterobacteriaceae (Micronaut-E, MERLIN-Diagnostika, Bornheim, Germany) and a rapid identification system for gram-negative and gram-positive bacteria (Micronaut-IDS, MERLIN-Diagnostika). Both identification systems test key biochemical reactions of bacteria with clinical significance. The inoculum for the identification tests was a suspension from an overnight culture on solid medium in physiological saline solution at 10^6 cfu/ml for the Micronaut E system and 10^8 cfu/ml for the Micronaut-IDS system. The incubation times were 24 h (Micronaut-E and agar plates) or 5 h (Micronaut-IDS) at 36°C (±1°). Fermentation of D-galactose was tested on bromocresol purple agar (Difco) supplemented with galactose 6 g/L. All identification tests were repeated to confirm the results.

Antibiotic susceptibility testing

Antibiotic susceptibility was tested by a microdilution procedure in Isosensitest Broth (Oxoid). After inoculation of antibiotic containing microtitration plates (MERLIN-Diagnostika) with 100 µl of appropriate bacterial suspension (~10^5 cfu/ml) and incubation for 24 h at 36°C (±1°) MIC values were determined with a photometer (Labsystems Multiskan Multisoft). MIC data were evaluted with EXCEL (Microsoft).

Evaluation of natural antibiotic susceptibility

Plotting the MIC of a particular antibiotic for one species against the number of strains found with the respective MIC usually results in a bimodal distribution. One peak with relatively low MICs represents the natural population and one peak with higher MICs represents the strains with acquired (secondary) resistance. Analysis of the MIC distribution of all strains of one species for each antibiotic permitted determination of the biological thresholds, which limit the natural population at high MICs but not those strains with secondary (acquired) resistance (Fig. 1a and b). Whether the MIC values of the natural population were above or below the breakpoints of the standards, which assess the clinical susceptibility was investigated. Determination of whether the natural population was clinically sensitive, intermediate or resistant was by application of French (SFM), Swedish (SIR), German (DIN), American (NCCLS) and English standards (BSAC). When the natural population was sensitive or intermediate according to the cited standards, it was described as naturally sensitive (Fig. 1a) or naturally intermediate, respectively. When the natural population was resistant, it was described as naturally (primary or intrinsically) resistant (Fig. 1b).

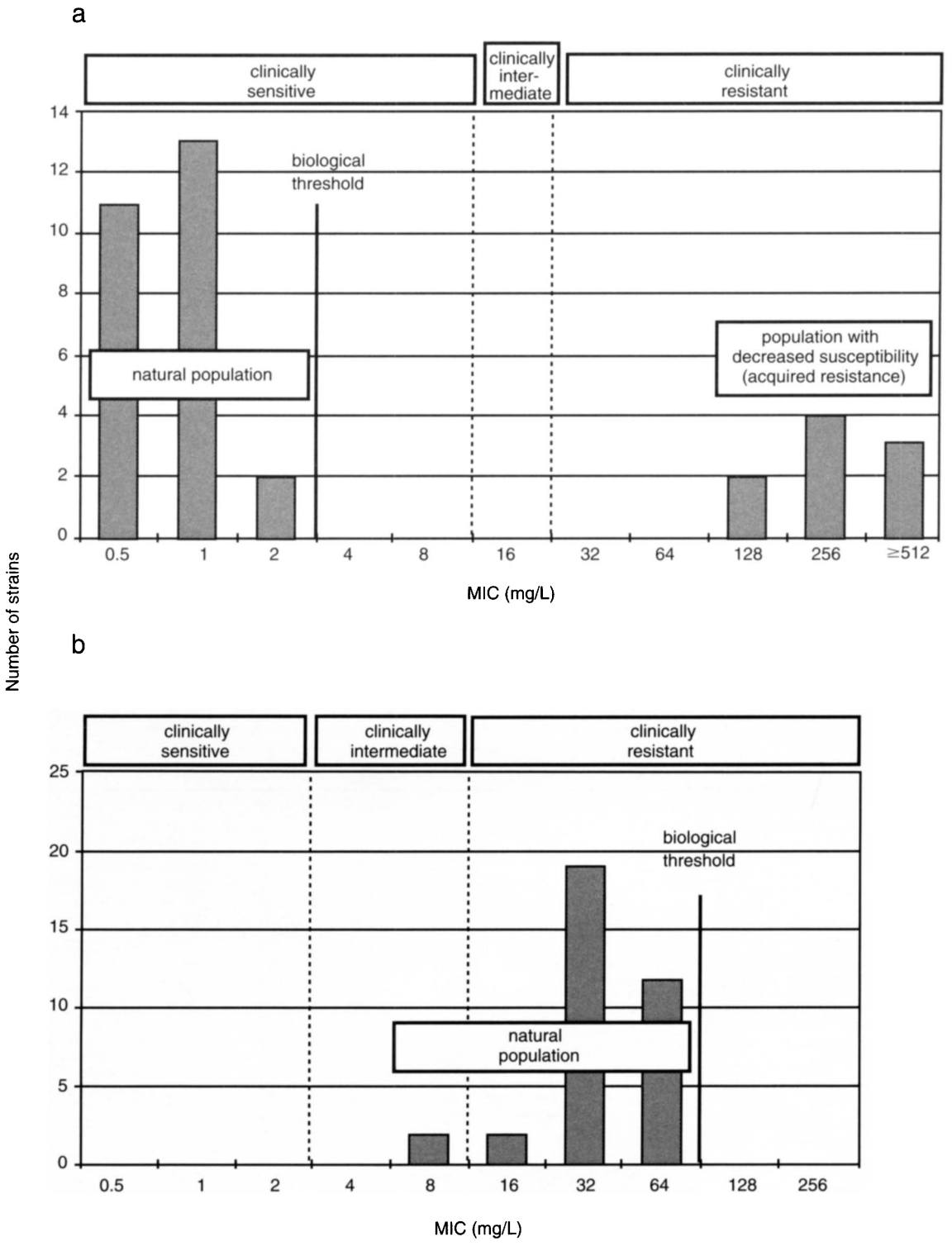

Fig. 1. (**a**) Susceptibility of *P. stuartii* to kanamycin. The biological threshold limits the natural population at high MICs excluding the strains with acquired resistance (population with decreased susceptibility). The biological threshold of *P. stuartii* for kanamycin was 2 mg/L. The MIC values of the acquired resistant population were 128– > 256 mg/L (see Table 2). The clinical assessment of MIC data is shown according to French standards (SFM). Clinical thresholds are indicated by dotted lines. *P. stuartii* was naturally sensitive to kanamycin, as the natural population was clinically sensitive according to SFM. (**b**) Susceptibility of *P. stuartii* towards amoxycillin in combination with clavulanic acid (AMX/CLAV). The biological threshold of *P. stuartii* for AMX/CLAV was 64 mg/L. Strains with acquired resistance were not found (see Table 2). The clinical assessment of MIC data is shown according to German standards (DIN). *P. stuartii* was naturally resistant to AMX/CLAV, as the natural population was clinically resistant according to DIN.

Results

Identification of strains

The biochemical features of the *Providencia* strains examined are shown in Table 1. Thirty-five strains were identified as *P. stuartii*, 38 as *P. rettgeri*, 23 as *P. alcalifaciens* and 20 as *P. rustigianii*. Generally, there were no significant differences between the results and those reported by Farmer [15], although the results of mannose and trehalose fermentation were read in the Micronaut-IDS system after 5 h whereas Farmer read these results after incubation for 2 days. Aesculin hydrolysis, urease production, fermentation of rhamnose, adonitol, myo-inositol, trehalose, D-galactose and the nagase and phosphodiesterase tests (cleavage of *p*-nitrophenyl-acetylglucosamine and 2′-deoxythymidine-5′-*p*-nitrophenylphosphate, respectively) were the most suitable tests to distinguish the *Providencia* spp. (Table 1).

Natural antibiotic sensitivity and primary resistance

The MIC distributions of the *Providencia* strains tested are presented in Table 2. There were significant differences in antibiotic susceptibility between the different *Providencia* spp. Antibiotics with discriminating features for *Providencia* spp. included tetracyclines and fosfomycin. A summary of the natural antibiotic sensitivities and primary resistances of *Providencia* spp. is shown in Table 3. Strains with acquired resistance were found in all species (Table 2).

Discussion

P. stuartii has been called a multiresistant species [1]. It was found, that *P. stuartii* was naturally resistant to a wide range of antibiotics, e.g., tetracyclines, some penicillins and older cephalosporins, to which some

Table 1. Biochemical features of *Providencia* spp.

	Positive reactions (%)							
	P. rettgeri		*P. stuartii*		*P. alcalifaciens*		*P. rustigianii*	
Biochemical test	I	II	I	II	I	II	I	II
1. Amino acid deaminase[0]	100	98	97	96	100	98	100	100
2. Hydrogen sulphide production	0	0	3	0	0	0	0	0
3. **β-Glucosidase**[1]	**68**	35	**0**	0	**0**	0	**25**	0
4. Tryptophanase[2]	92	99	97	98	87	99	95	98
5. **Urease**	**95**	98	**40**	30	**0**	0	**0**	0
6. Lysine decarboxylase	0	0	0	0	0	0	0	0
7. Ornithine decarboxylase	0	0	0	0	0	1	0	0
8. Arginine dihydrolase	0	0	0	0	0	0	0	0
9. Glucose fermentation	100	100	100	100	100	100	100	100
10. Citrate assimilation[3]	100	95	100	93	100	98	100	15
11. Malonate assimilation	0	0	0	0	0	0	10	0
12. Voges Proskauer reation	0	0	0	0	0	0	0	0
13. **Rhamnose fermentation**	**45**	70	**0**	0	**0**	0	**0**	0
14. Sucrose fermentation	3	15	29	50	0	15	0	35
15. **Adonitol fermentation**	**100**	100	**0**	5	**100**	98	**0**	0
16. **(Myo)-inositol fermentation**	**100**	90	**94**	95	**0**	1	**0**	0
17. Xylose fermentation	8	10	6	7	13	1	25	0
18. Sorbitol fermentation	0	1	0	1	0	1	0	0
19. β-Galactosidase[4]	3	5	0	10	0	1	0	0
20. β-Xylosidase[5]	0	ns	0	ns	0	ns	0	ns
21. β-Glucuronidase[6]	0	ns	0	ns	0	ns	0	ns
22. Proline amidase	0	ns	0	ns	0	ns	0	ns
23. Pyrase	0	ns	0	ns	0	ns	0	ns
24. Hydroxyproline amidase	0	ns	0	ns	0	ns	0	ns
25. Peptidase	0	ns	0	ns	0	ns	0	ns
26. α-Glucosidase	3	ns	0	ns	0	ns	0	ns
27. **Nagase** (chitinase)[7]	**0**	ns	**100**	ns	**17**	ns	**10**	ns
28. α-Galactosidase	0	ns	0	ns	0	ns	0	ns
29. **Phosphodiesterase**[8]	**76**	ns	**0**	ns	**61**	ns	**15**	ns
30. L-Alanine aminopeptidase	100	ns	100	ns	100	ns	100	ns
31. Mannose fermentation	100	100	100	100	100	100	100	100
32. **Trehalose fermentation**	**0**	0	**97**	98	**0**	2	**0**	0
33. **D-Galactose fermentation**	**100**	ns	**100**	ns	**0**	ns	**100**	ns

The results (I) are contrasted with the data of Farmer (II) [15]. Most of the reactions were either included in the panels of the Micronaut-E (1–21.) or the Micronaut-IDS identification system of MERLIN (22–32).

Key discriminating reactions are given in bold print. [0]tryptophan deaminase (MERLIN), phenylalanine deaminase [Farmer]; [1]hydrolysis of aesculin; [2]indole production; [3]mixture of Simmons' and Christensen citrate (MERLIN), Simmons' citrate [Farmer]; cleavage of [4]ortho-nitrophenyl-β-galactopyranoside (ONPG), [5]ortho-nitrophenyl-β-xyloside (ONPX), [6]para-nitrophenyl-β-glucuronide (PGUR), [7]para-nitrophenyl-acetylglucosamine, [8]2′-deoxythymidine-5′-para-nitrophenylphosphate; ns, not stated.

Table 2. Antibiotic susceptibility of *P. stuartii*, *P. rettgeri*, *P. alcalifaciens* and *P. rustigianii*

Antibiotic	Species	Number of strains and MIC distribution (antibiotic concentration mg/L)																
		0.01	0.03	0.06	0.13	0.3	0.5	1	2	4	8	16	32	64	128	256	512	1024
Tetracylines	*P. stuartii*														35			
Tetracycline	*P. rettgeri*									1	3	2			32			
(0.03–64)	*P. alcalifaciens*							2	3	6	2				10			
	P. rustigianii							1	11	4	2				2			
Doxycycline	*P. stuartii*														35			
(0.03–64)	*P. rettgeri*										2		4		32			
	P. alcalifaciens					1		1	2	6	2	1			10			
	P. rustigianii							1	11	4	2				2			
Minocycline	*P. stuartii*										1	3	12	10	9			
(0.03–64)	*P. rettgeri*									4	11	14	4	4	1			
	P. alcalifaciens						1	1	3	5	5	2	6					
	P. rustigianii						1	3	9	4	1		2					
Aminoglycosides	*P. stuartii*						8	19	8									
Amikacin	*P. rettgeri*						12	21	3		1			1				
(0.13–256)	*P. alcalifaciens*						4	10	5	1	1	1	1					
	P. rustigianii						1	12	5	2								
Gentamicin	*P. stuartii*							13	10	4	4	2	1		1			
(0.06–128)	*P. rettgeri*					9	12	9	7				1					
	P. alcalifaciens				3	7	9	2						2				
	P. rustigianii				1	10	5	1	3									
Netilmicin	*P. stuartii*							1	14	11	4	2		1	1	1		
(0.06–128)	*P. rettgeri*				1	7	15	7	7	1								
	P. alcalifaciens				3	8	6		3		1			1	1			
	P. rustigianii				3	8	5	2	1	1								
Tobramycin	*P. stuartii*							7	15	6	2	2	1	2				
(0.06–128)	*P. rettgeri*					9	15	7	5	1		1						
	P. alcalifaciens				2	11	3	3	2			1	1					
	P. rustigianii				1	12	3	2	1	1								
Streptomycin	*P. stuartii*									5	12	11	2		2		3	
(0.13–256)	*P. rettgeri*						1		20	7	7			1	1		1	
	P. alcalifaciens							2	10	4	2			2	1	2		
	P. rustigianii							2	9	5		3					1	
Kanamycin	*P. stuartii*						11	13	2						2	4	3	
(0.13–256)	*P. rettgeri*						11	18	6	1					1		1	
	P. alcalifaciens						3	12	2	4		1	1					
	P. rustigianii						5	12	1	1		1						
Neomycin	*P. stuartii*							6	11	7	2	3	2	1	1		2	
(0.13–256)	*P. rettgeri*						3	14	14	1	2	1	2				1	
	P. alcalifaciens					1	12	4	3	1				1	1			
	P. rustigianii					1	10	5	2	2								
Spectinomycin	*P. stuartii*												1	2	2	7	23	
(0.13–256)	*P. rettgeri*										3	8	4	1	9	5	8	
	P. alcalifaciens										2	10	5	1	3	1	1	
	P. rustigianii										2	14	2			2		

continued overleaf

Table 2. (*continued*)

Antibiotic	Species	Number of strains and MIC distribution (antibiotic concentration mg/L)																
		0.01	0.03	0.06	0.13	0.3	0.5	1	2	4	8	16	32	64	128	256	512	1024
Apramycin	*P. stuartii*						2	16	12	4	1							
(0.06–128)	*P. rettgeri*						2	15	15	5	1							
	P. alcalifaciens						1	10	8	1	1			1	1			
	P. rustigianii						3	6	8	1	2							
Ribostamycin	*P. stuartii*										2	7	8	7	1	10		
(0.06–128)	*P. rettgeri*							1	2	6	6	14	5	2		2		
	P. alcalifaciens							5	10	1	2	2	2	1				
	P. rustigianii						1	4	7	4	3		1					
Lividomycin A	*P. stuartii*								1	5	8	6	2	2		11		
(0.06–128)	*P. rettgeri*								5	11	11	8	1			2		
	P. alcalifaciens								8	9	3	1				2		
	P. rustigianii							1	3	12	1	3						
Penicillins	*P. stuartii*												6	29				
Benzylpenicillin	*P. rettgeri*				1			2	2	6	3	4	6	14				
(0.01–32)	*P. alcalifaciens*									3	3	7	5	5				
	P. rustigianii								2	10	7			1				
Oxacillin	*P. stuartii*												6	12	17			
(0.03–64)	*P. rettgeri*									2	12	18	4		2			
	P. alcalifaciens									1	2	11	5	4				
	P. rustigianii										5	11	2	1	1			
Amoxycillin	*P. stuartii*												6	9	9	11		
(0.06–128)	*P. rettgeri*						4	4	3	3	3	3	7	4	1	6		
	P. alcalifaciens									1	2	4	4	4	2	6		
	P. rustigianii							1	6	5	4	2	1		1			
Amoxycillin/	*P. stuartii*										2	2	19	12				
clavulanic acid	*P. rettgeri*					3		1	2	5	5	14	6	1	1			
(0.06–128)	*P. alcalifaciens*			1				1	3	2	3	8	4	1				
	P. rustigianii							2	5	7	3	1	1	1				
Ampicillin/	*P. stuartii*									1	15	18	1					
sulbactam	*P. rettgeri*					1	2	5	1	4	6	14	3	1		1		
(0.06–128)	*P. alcalifaciens*					1		4	4	3	4	7						
	P. rustigianii						1	5	8	5		1						
Piperacillin	*P. stuartii*							6	13	4	1		2	1	4	1	3	
(0.13–256)	*P. rettgeri*					14	14	4	4						1	1		
	P. alcalifaciens						3	7	3	7	3							
	P. rustigianii						1	16	2	1								
Piperacillin/	*P. stuartii*						12	14	9									
tazobactam	*P. rettgeri*					14	23										1	
(0.13–256)	*P. alcalifaciens*				2	10	9	2										
	P. rustigianii						11	9										
Ticarcillin	*P. stuartii*					4	11	5	2	1			1	1	1	4	5	
(0.13–256)	*P. rettgeri*					12	16	2	1		1		4			1	1	
	P. alcalifaciens					2	5	1	2	3	3	2		2	2	1		
	P. rustigianii					12	7	1										
Mezlocillin	*P. stuartii*							1	9	13	1		2	1	2	3	3	
(0.13–256)	*P. rettgeri*						1	17	15	3						2		
	P. alcalifaciens					1			7	9	5	1						
	P. rustigianii							1	15	4								

Table 2. (*continued*)

Antibiotic	Species	Number of strains and MIC distribution (antibiotic concentration mg/L)																
		0.01	0.03	0.06	0.13	0.3	0.5	1	2	4	8	16	32	64	128	256	512	1024
Azlocillin	*P. stuartii*									4	8	8	2	1	2	6	3	1
(0.25–512)	*P. rettgeri*							6	12	12	6					1		1
	P. alcalifaciens								2	7	5	6	3					
	P. rustigianii								1	11	7				1			
Cephalosporins	*P. stuartii*										2	3	7	11	6	6		
Cefaclor	*P. rettgeri*			1	1	2	2	4	2	6	3	1	2	3	4	7		
(0.06–128)	*P. alcalifaciens*					3	2	1	4	1	4	2	1	1	2	2		
	P. rustigianii					1	3	6	4	2	3					1		
Cefazoline	*P. stuartii*								1	2				1	1	17	13	
(0.13–256)	*P. rettgeri*				7	7	4			3	1	2	2	2	2	2	6	
	P. alcalifaciens				1	4	5			2	1	1	1	1	7			
	P. rustigianii				1	8	6	2	2						1			
Loracarbef	*P. stuartii*								1	1	3	5	13	4	6		2	
(0.13–256)	*P. rettgeri*				1	3	4	3	1	1	5	2	6	6	4	1	1	
	P. alcalifaciens				2	4	3	1	1	2	2	1	2	3	1	1		
	P. rustigianii					6	5	4	4					1				
Cefuroxime	*P. stuartii*						2	4	11	11	5			1	1			
(0.03–64)	*P. rettgeri*			1	11	15	7	2		1				1				
	P. alcalifaciens				3	12	2			1	3	1			1			
	P. rustigianii				1	3	15							1				
Cefotiam	*P. stuartii*		4	1	8	10	6	3					2	1				
(0.03–64)	*P. rettgeri*		31	1	1	1	2			1					1			
	P. alcalifaciens		10	6	1			1				3	2					
	P. rustigianii		7	12								1						
Cefetamet	*P. stuartii*		24	3	4	1		2	1									
(0.03–64)	*P. rettgeri*		36		1			1										
	P. alcalifaciens		18	1	1				3									
	P. rustigianii		19				1											
Cefoxitin	*P. stuartii*							14	16	2	2		1					
(0.03–64)	*P. rettgeri*							16	13	5	3				1			
	P. alcalifaciens							3	10	7	2		1					
	P. rustigianii							11	8		1							
Cefixim	*P. stuartii*		21	8	3	1	1				1							
(0.03–64)	*P. rettgeri*		36	1				1										
	P. alcalifaciens		17	1		2			1	1	1							
	P. rustigianii		19			1												
Cefpodoxime	*P. stuartii*		8	11	6	5	1	1		2			1					
(0.03–64)	*P. rettgeri*		34	2	1					1								
	P. alcalifaciens		17		1		1	1		3								
	P. rustigianii		19							1								
Cefdinir	*P. stuartii*		9	5	11	4	3											
(0.03–64)	*P. rettgeri*		32	4	1													
	P. alcalifaciens		16	1		1	1	1										
	P. rustigianii		18	1														

continued overleaf

Table 2. (*continued*)

Antibiotic	Species	Number of strains and MIC distribution (antibiotic concentration mg/L)																
		0.01	0.03	0.06	0.13	0.3	0.5	1	2	4	8	16	32	64	128	256	512	1024
Cefoperazone	*P. stuartii*					1	1	7	6	7	8	4	1					
(0.03–64)	*P. rettgeri*				6	12	8	6	5				1					
	P. alcalifaciens					5	10	3		1	2	1		1				
	P. rustigianii						7	11	1		1							
Cefotaxime	*P. stuartii*		14	7	6	3	2	1	2									
(0.03–64)	*P. rettgeri*		36		1					1								
	P. alcalifaciens		17	1		1	1		1	2								
	P. rustigianii		19						1									
Ceftibutene	*P. stuartii*		33		1						1							
(0.03–64)	*P. rettgeri*		37								1							
	P. alcalifaciens		18			1					2	1	1					
	P. rustigianii		20															
Ceftriaxone	*P. stuartii*		29	3		2		1										
(0.03–64)	*P. rettgeri*		37							1								
	P. alcalifaciens		18				2	3										
	P. rustigianii		19		1													
Ceftazidime	*P. stuartii*			4	13	13	4			1								
(0.03–64)	*P. rettgeri*		20	10	6	1								1				
	P. alcalifaciens		3	10	4	2		1	1	2								
	P. rustigianii			1	7	11	1											
Cefepime	*P. stuartii*		23	8	2	1	1											
(0.03–64)	*P. rettgeri*		34	2		1								1				
	P. alcalifaciens		18					1	3	1								
	P. rustigianii		19				1											
Carbapenems	*P. stuartii*					2	11	18	3	1								
Imipenem	*P. rettgeri*					7	12	14	4						1			
(0.03–64)	*P. alcalifaciens*				1	4	13	4			1							
	P. rustigianii				7	10	3											
Meropenem	*P. stuartii*		19	14	1		1											
(0.03–64)	*P. rettgeri*		16	19	2						1							
	P. alcalifaciens		11	8	1	3												
	P. rustigianii		19	1														
Biapenem	*P. stuartii*			4	2	6	19	3		1								
(0.03–64)	*P. rettgeri*				5	15	15	2					1					
	P. alcalifaciens				8	10	4	1										
	P. rustigianii		3	16	1													
Monobactams	*P. stuartii*		34				1											
Aztreonam	*P. rettgeri*		37										1					
(0.03–64)	*P. alcalifaciens*		18						1	2	1	1						
	P. rustigianii		20															
Quinolones	*P. stuartii*	7	6	4	2	7	1	2	3	1	1			1				
Ciprofloxacin	*P. rettgeri*	15	17	2					1	2	1							
(0.01–32)	*P. alcalifaciens*	6	7	4	4	1	1											
	P. rustigianii	8	9	2										1				
Sparfloxacin	*P. stuartii*		4	8	6	2	4	7	2	1		1						
(0.01–32)	*P. rettgeri*		2	16	9	4	3				3	1						
	P. alcalifaciens		3		3	5	4	6	1	1								
	P. rustigianii	3	3	13							1							

Table 2. (*continued*)

Antibiotic	Species	Number of strains and MIC distribution (antibiotic concentration mg/L)																
		0.01	0.03	0.06	0.13	0.3	0.5	1	2	4	8	16	32	64	128	256	512	1024
Norfloxacin	*P. stuartii*			7	7	4	5	1	4	4	1	1		1				
(0.03–64)	*P. rettgeri*			12	20	2				1	1	1	1					
	P. alcalifaciens			9	8		2	1	2		1							
	P. rustigianii			3	12	3	1								1			
Ofloxacin	*P. stuartii*				10	5	6	5	3	3	2			1				
(0.01–32)	*P. rettgeri*			1	18	14	1				4							
	P. alcalifaciens			3	7	9	3		1									
	P. rustigianii			3	14	2								1				
Enoxacin	*P. stuartii*					12	6	5	4	3	2	1	1	1				
(0.01–32)	*P. rettgeri*				4	27	3					3	1					
	P. alcalifaciens				2	15	2	3		1								
	P. rustigianii					16	3							1				
Fleroxacin	*P. stuartii*			1	13	6	2	4	5	2	1	1						
(0.01–32)	*P. rettgeri*			15	17	2				4								
	P. alcalifaciens			5	14	2	1		1									
	P. rustigianii			6	13								1					
Pefloxacin	*P. stuartii*				11	8	4	2	6		3			1				
(0.01–32)	*P. rettgeri*			1	24	9					4							
	P. alcalifaciens			2	13	5	2		1									
	P. rustigianii			3	14	2								1				
Pipemid acid	*P. stuartii*							1	7	10	6	4	3	1	2	1		
(0.06–128)	*P. rettgeri*							3	26	3	1	1			3	1		
	P. alcalifaciens								15	3		4	1					
	P. rustigianii								3	14	2					1		
Macrolides	*P. stuartii*														35			
Erythromycin	*P. rettgeri*													1	37			
(0.03–64)	*P. alcalifaciens*												1		22			
	P. rustigianii													1	19			
Roxithromycin	*P. stuartii*														35			
(0.03–64)	*P. rettgeri*														38			
	P. alcalifaciens													1	22			
	P. rustigianii														20			
Clarithromycin	*P. stuartii*													3	32			
(0.03–64)	*P. rettgeri*												1	4	33			
	P. alcalifaciens												1	4	18			
	P. rustigianii													1	19			
Azithromycin	*P. stuartii*												6	20	9			
(0.03–64)	*P. rettgeri*											3	4	20	11			
	P. alcalifaciens							1				2	9	7	4			
	P. rustigianii											1	12	7				
Lincosamides	*P. stuartii*													35				
Lincomycin	*P. rettgeri*													38				
(0.01–32)	*P. alcalifaciens*													23				
	P. rustigianii													20				

continued overleaf

Table 2. (*continued*)

Antibiotic	Species	Number of strains and MIC distribution (antibiotic concentration mg/L)																
		0.01	0.03	0.06	0.13	0.3	0.5	1	2	4	8	16	32	64	128	256	512	1024
Clindamycin	*P. stuartii*													35				
(0.01–32)	*P. rettgeri*													38				
	P. alcalifaciens												1	22				
	P. rustigianii												1	19				
Streptogramins	*P. stuartii*														35			
Dalfopristin	*P. rettgeri*														38			
(0.03–64)	*P. alcalifaciens*														23			
	P. rustigianii														20			
Quinopristin	*P. stuartii*														35			
(0.03–64)	*P. rettgeri*														38			
	P. alcalifaciens														23			
	P. rustigianii														20			
Synercid	*P. stuartii*														35			
(0.03–64)	*P. rettgeri*														38			
	P. alcalifaciens													1	22			
	P. rustigianii														20			
Co-trimoxazole group	*P. stuartii*										1			2	2		3	27
Sulphamethoxazole	*P. rettgeri*										1	1	1					35
(0.25–512)	*P. alcalifaciens*										2	4	3	7	2	2		3
	P. rustigianii										1						7	12
Trimethoprim	*P. stuartii*							6	6	6		3	1		13			
(0.03–64)	*P. rettgeri*						5	14	8	3			1		7			
	P. alcalifaciens				4	5	3	1	2	2		3	1		2			
	P. rustigianii			2	9	6	1	1		1								
Co-trimoxazole	*P. stuartii*								7	8	1	2	2	2	1		12	
(0.13–256)	*P. rettgeri*							1	13	10	5		2	2		1	4	
	P. alcalifaciens						1	11	4	2		1		1		2	1	
	P. rustigianii						5	11	3			1						
Glycopeptides	*P. stuartii*															35		
Teicoplanin	*P. rettgeri*															38		
(0.06–128)	*P. alcalifaciens*															23		
	P. rustigianii															20		
Vancomycin	*P. stuartii*														35			
(0.03–64)	*P. rettgeri*														38			
	P. alcalifaciens														23			
	P. rustigianii														20			
Other antibiotics	*P. stuartii*									5	8	7	6	3	3	3		
Chloramphenicol	*P. rettgeri*									1	13	14	7		1	2		
(0.06–128)	*P. alcalifaciens*						1		1	10	6	5						
	P. rustigianii									8	8	2	1			1		
Nitrofurantoin	*P. stuartii*												1	2	17	12	3	
(0.13–256)	*P. rettgeri*														7	24	7	
	P. alcalifaciens												2	15	4	2		
	P. rustigianii													3	17			
Rifampicin	*P. stuartii*									9	23	3						
(0.01–32)	*P. rettgeri*									8	20	10						
	P. alcalifaciens								1	1	1	18	1	1				
	P. rustigianii									2	9	9						

Table 2. (*continued*)

Antibiotic	Species	Number of strains and MIC distribution (antibiotic concentration mg/L)														
		0.01	0.03	0.06	0.13	0.3	0.5	1	2	4	8	16	32	64	128	256	512	1024
Fosfomycin (0.013–256)	*P. stuartii*																35	
	P. rettgeri												8	5	9	7	9	
	P. alcalifaciens									1	1	2	9	7		1	2	
	P. rustigianii									2	3	11	2				2	
Fusidic acid (0.01–32)	*P. stuartii*													35				
	P. rettgeri													38				
	P. alcalifaciens													23				
	P. rustigianii													20				

The antibiotic concentrations tested (mg/L) are stated in parenthesis below the corresponding drugs. A number in the lowest concentration of the antibiotic represents the maximal MIC value (MIC = c_{min} → MIC ≤ c_{min}). An MIC value higher than the highest concentration tested is shown in the subsequent higher concentration step. MIC values in shaded areas indicate the clinically intermediate area according to the German standard (DIN). A black thick line indicates the breakpoint between the clinically sensitive and clinically resistant strains, when an intermediate sensitivity does not exist. If the DIN clinical assessment criteria for an antibiotic did not occur, other standards were employed. Breakpoints according to American standards (NCCLS) were used for spectinomycin, sulphamethoxazole, teicoplanin and rifampicin; French (SFM) and Swedish standards (SIR) were utilised for kanamycin, neomycin, sparfloxacin, pefloxan, lincomycin, fosfomycin and for roxithromycin, clarithromycin, trimethoprim and fusidic acid, respectively. The British standard (BSAC) was employed for meropenem. It is taken into account that this standard is based on an agar dilution technique. No clinical assessment criteria exist for streptomycin, apramycin, ribostamycin, lividomycin A, cefdinir, biapenem, dalfopristin, quinopristin and synercid.

other species of Enterobacteriaceae were naturally sensitive or naturally of intermediate susceptibility. However, there was also a range of antibiotics, such as modern penicillins and cephalosporins, carbapenems and aztreonam, to which the species was naturally sensitive. The natural susceptibility pattern to some antibiotics, especially aminoglycosides and quiniolones, was difficult to assess. The MIC distributions of quinolones did not correspond to standard distributions and unequivocal clinical interpretations of the data could not be made. Although clinical interpretations of the MIC distributions of aminoglycosides seemed to be established easily, *P. stuartii* should be regarded as naturally resistant to certain aminoglycosides (see below).

According to the data, *P. alcalifaciens* and *P. rustigianii* were the most susceptible *Providencia* spp. They were naturally sensitive or naturally of intermediate susceptibility to tetracyclines and sensitive to aminoglycosides and quinolones. Both species were also naturally sensitive to antibiotics to which *P. stuartii* was naturally sensitive. Susceptibility to sparfloxacin, biapenem and sulphamethoxazole were suitable parameters for the discrimination of *P. alcalifaciens* and *P. rustigianii* (Tables 2 and 3). The natural antibiotic susceptibility patterns of *P. rettgeri* were between those of *P. stuartii* and those of the other *Providencia* spp. Like *P. stuartii, P. rettgeri* was resistant to tetracyclines and fosfomycin, but was more susceptible to aminoglycosides, quinolones, fosfomycin and numerous β-lactam antibiotics (Tables 2 and 3).

Most resistance mechanisms (including natural resistance) to antimicrobial agents in *Providencia* spp. are unknown. This is particularly true for species other than *P. stuartii*. Resistance to aminoglycosides is mostly attributed to the action of aminoglycoside-modifying enzymes. In *P. stuartii*, natural resistance to aminoglycosides is limited to aminoglycosides of the gentamicin type (gentamicin, tobramycin and netilmicin) and is due to a chromosomally encoded 2′-N-acetyltransferase, designed AAC(2′)-Ia, which is distributed ubiquitously in this species [16]. According to the present data *P. stuartii* was sensitive, intermediate or slightly resistant (depending on the applied standard) to gentamicin (Table 3), but there was no uniform resistance. Otherwise, the species showed significantly less susceptibility to gentamicin, tobramycin and netilmicin than the other *Providencia* spp. (Table 2). It has been shown that the acetyltransferase is normally expressed at low levels, but high-level expression confers resistance to gentamicin and structurally related aminoglycosides [16]. However, the MIC data did not confirm that the AAC(2′)-Ia enzyme was also present in *P. rettgeri*, as has been described [17, 18].

Excluding resistance to oxacillin, and presumably benzylpenicillin, natural resistance to β-lactam agents in *Providencia* strains is probably due to inducible

Table 3. Grouping of the natural population of *P. stuartii*, *P. rettgeri*, *P. alcalifaciens* and *P. rustigianii* into the categories sensitive, intermediate and resistant

Antibiotic group	Antibiotic	Taxon	Naturally sensitive					Naturally intermediate					Naturally resistant				
			F	S	G	U	B	F	S	G	U	B	F	S	G	U	B
Tetracyclines	Tetracycline	*P. stuartii*											x	x	x	x	x
		P. rettgeri						x			x			x	x		x
		P. alcalifaciens, *P. rustigianii*	x			x	x		x	x				x			x
	Doxycycline	*P. stuartii*, *P. rettgeri*											x	x	x		x
		P. alcalifaciens, *P. rustigianii*	x				x		x	x				x			x
	Minocycline	*P. stuartii*											x		x		x
		P. rettgeri	x					x					x		x		x
		P. alcalifaciens	x				x	x		x			x		x		x
		P. rustigianii	x				x			x							x
Aminoglycosides	Amikacin	All species	x	x	x	x	x										
	Gentamicin	*P. stuartii*	x	x	x	x	x	x		x	x	x		x	x		x
		P. rettgeri	x	x	x	x	x			x		x					
		P. alcalifaciens, *P. rustigianii*	x	x	x	x	x										
	Netilmicin	*P. stuartii*	x	x		x	x	x		x		x		x	x		x
		P. rettgeri	x	x	x	x	x			x		x					
		P. alcalifaciens, *P. rustigianii*	x	x	x	x	x										
	Tobramycin	*P. stuartii*	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x
		P. rettgeri	x	x	x	x	x			x		x					
		P. alcalifaciens, *P. rustigianii*	x	x	x	x	x										
	Kanamycin	All species	x			x											
	Neomycin	*P. stuartii*	x					x					x				
		P. rettgeri	x					x									
		P. alcalifaciens, *P. rustigianii*	x														
	Spectinomycin	*P. stuartii*														x	
		P. rettgeri				x										x	
		P. alcalifaciens, *P. rustigianii*				x											
Penicillins	Benzylpenicillin	*P. stuartii*											x	x	x	x	
		P. rettgeri						x	x		x		x	x	x	x	
		P. alcalifaciens						x	x				x	x	x	x	
		P. rustigianii						x	x					x	x	x	
	Oxacillin	All species												x	x	x	
	Amoxycillin	*P. stuartii*											x	x	x	x	x
		P. rettgeri	x	x	x	x	x	x	x	x	x		x	x	x	x	x
		P. alcalifaciens				x	x	x	x	x	x		x	x	x	x	x
		P. rustigianii	x		x	x	x	x	x	x	x			x	x		x
	AMX/CLAV	*P. stuartii*						x			x		x	x	x	x	x
		All species except *P. stuartii*	x		x	x	x	x	x	x	x		x	x	x	x	x
	AMP/SUL	*P. stuartii*				x	x	x	x	x	x			x	x		x
		P. rettgeri	x	x	x	x	x	x	x	x	x		x	x	x	x	x
		P. alcalifaciens	x	x	x	x	x	x	x	x	x			x	x		x
		P. rustigianii	x	x	x	x	x		x	x							
	Piperacillin	All species except *P. alcalifaciens*	x	x	x	x	x										
		P. alcalifaciens	x	x	x	x	x			x							
	PIP/TAZ	All species	x	x	x	x	x										
	Ticarcillin	All species except *P. alcalifaciens*	x		x	x	x										
		P. alcalifaciens	x		x	x	x			x							
	Mezlocillin	All species except *P. alcalifaciens*	x	x	x	x	x										
		P. alcalifaciens	x	x	x	x	x			x							
	Azlocillin	*P. stuartii*			x	x	x			x		x			x	x	x
		P. rettgeri, *P. rustigianii*			x	x	x										
		P. alcalifaciens			x	x	x			x		x					
Cephalosporins	Cefaclor	*P. stuartii*									x		x	x	x	x	
		P. rettgeri, *P. alcalifaciens*	x	x	x	x		x	x	x	x		x	x	x	x	
		P. rustigianii	x	x	x	x		x	x	x					x		
	Cefazoline	*P. stuartii*													x	x	
		P. rettgeri, *P. alcalifaciens*			x	x				x	x				x	x	
		P. rustigianii			x	x											
	Loracarbef	*P. stuartii*				x		x		x	x		x		x	x	
		P. rettgeri, *P. alcalifaciens*	x		x	x		x		x	x		x		x	x	
		P. rustigianii	x		x	x											
	Cefuroxime	All species except *P. stuartii*	x	x	x	x	x										
		P. stuartii	x	x	x	x	x			x		x					
	Cefotiam	All species	x		x	x											
	Cefetamet	All species	x	x			x										
	Cefoxitin	*P. rustigianii*	x	x	x	x											
		All species except *P. rustigianii*	x	x	x	x				x							
	Cefixim	All species	x		x	x	x										
	Cefpodoxime	All species	x	x	x	x	x										
	Cefoperazone	All species except *P. stuartii*	x		x	x											
		P. stuartii	x		x	x				x							
	Cefotaxime	All species	x	x	x	x	x										
	Ceftibutene	All species	x		x	x											

Table 3. (*continued*)

Antibiotic group	Antibiotic	Taxon	Naturally sensitive					Naturally intermediate					Naturally resistant				
			F	S	G	U	B	F	S	G	U	B	F	S	G	U	B
	Ceftriaxone	All species	x		x	x											
	Ceftazidime	All species	x	x	x	x	x										
	Cefepime	All species	x		x	x											
Carbapenems	Imipenem	All species	x	x	x	x	x										
	Meropenem	All species	x				x										
Monobactams	Aztreonam	All species	x	x	x	x	x										
Quinolones	Ciprofloxacin	All species except *P. stuartii*	x	x	x	x	x										
		P. stuartii	x	x	x	x	x	x	x	x	x	x					
	Sparfloxacin	*P. stuartii, P. alcalifaciens*	x					x									
		P. rettgeri, P. rustigianii	x														
	Norfloxacin	All species except *P. stuartii*	x	x	x	x	x										
		P. stuartii	x	x	x	x	x	x	x	x		x			x		x
	Ofloxacin	All species except *P. stuartii*	x	x	x	x	x										
		P. stuartii	x	x	x	x	x	x	x	x	x	x			x		
	Enoxacin	All species except *P. stuartii*	x		x	x	x										
		P. stuartii	x		x	x	x	x		x	x	x	x		x	x	x
	Fleroxacin	All species except *P. stuartii*			x	x											
		P. stuartii			x	x				x	x						
	Pefloxacin	All species except *P. stuartii*	x														
		P. stuartii	x					x									
	Pipemid acid	All species except *P. stuartii*	x		x								x		x		
		P. stuartii	x		x			x							x		
Macrolides	Erythromycin	All species											x	x	x	x	
	Roxithromycin	All species											x	x			
	Clarithromycin	All species											x	x		x	
	Azithromycin	All species											x		x	x	
Lincosamides	Lincomycin	All species											x				
	Clindamycin	All species											x	x	x	x	
Co-trimoxazole group	Sulphamethoxazole	All species except *P. alcalifaciens*														x	x
		P. alcalifaciens				x	x										x
	Trimethoprim	*P. stuartii*	x	x		x			x			x					x
		P. rettgeri, P. alcalifaciens	x	x		x	x		x			x					x
		P. rustigianii	x	x		x	x										
	Co-trimoxazole	All species	x	x	x	x											
Glycopeptides	Teicoplanin	All species											x			x	
	Vancomycin	All species											x	x	x	x	
Other antibiotics	Chloramphenicol	*P. stuartii, P. rettgeri*	x	x	x	x	x	x			x		x	x	x	x	x
		P. alcalifaciens, P. rustigianii	x	x	x	x	x	x			x			x	x		x
	Nitrofurantoin	*P. stuartii*			x			x		x	x		x	x	x	x	
		P. rettgeri						x		x			x	x	x	x	
		P. alcalifaciens		x	x	x		x		x	x		x	x	x	x	
		P. rustigianii			x			x			x			x	x	x	
	Rifampicin	All species except *P. alcalifaciens*	x					x						x		x	
		P. alcalifaciens	x					x					x	x		x	
	Fosfomycin	*P. stuartii*											x	x			
		P. rettgeri	x	x									x	x			
		P. alcalifaciens	x	x									x				
		P. rustigianii	x	x													
	Fusidic acid	All species												x			

Grouping was done according to French (SFM, abbreviated as F), Swedish, (SIR, S), German (DIN, G), American (NCCLS, U) and British standards (BSAC, B). If no x is shown, that country has not given standards for that antibiotic. It should be noted that British clinical assessment criteria are based on an agar dilution technique. Streptomycin, apramycin, ribostamycin, lividomycin A, cefdinir, biapenem, dalfopristin, quinopristin and synercid are not mentioned in this table, because clinical assessment criteria do not exist for these antibiotics. AMX/CLAV, amoxycillin/clavulanate; AMP/SUL, ampicillin/sulbactam; PIP/TAZ, piperacillin/tazobactam.

chromosomal β-lactamases, which are not yet characterised. Among providenciae the natural susceptibility to a wide range of β-lactam agents was difficult to determine, because the MIC ranges were often very broad (as was found with natural susceptibility to quinolones among *P. stuartii* strains). This was particularly true for aminopenicillins and some first and second generation cephalosporins (cefaclor, cefazolin and loracarbef), and also for ticarcillin against *P. alcalifaciens* (Table 2). Small variations in the inoculum size caused alterations of the MIC values over several concentration intervals. With an inoculum size of 10^6 cfu/ml, several strains of all species were also resistant to third and fourth generation cephalosporins, such as ceftazidime and cefepime (data not shown). However, results from repeated MIC determinations with a constant inoculum were also variable. This might be due to variable inducibility of β-lactamase expression in a *Providencia* strain. The molecular basis of this phenomenon remains to be elucidated.

The data represent an assessment of the natural susceptibility of strains of *Providencia* spp. to a wide

range of antibiotics. These databases can be used for the validation of antibiotic susceptibility test results of *Providencia* spp., especially with those antibiotics towards which the species are naturally resistant. If *Providencia* strains are found that are sensitive to these antibiotics, the antibiotic susceptibility testing should be repeated and the identification results confirmed.

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References

1. Hawkey PM. *Providencia stuartii*: a review of a multiply antibiotic-resistant bacterium. *J Antimicrob Chemother* 1984; **13**: 209–226.
2. Rinker AG, Boyd AL, Gary ND, Kundig W. Isolation of multiple antibiotic resistant Enterobacteriaceae from river water. *Microbios* 1988; **56**: 169–175.
3. Ladds PW, Bradley J, Hirst RG. *Providencia rettgeri* meningitis in hatchling saltwater crocodiles (*Crocodylus porosus*). *Aust Vet J* 1996; **74**: 397–398.
4. Albert MJ, Alam K, Ansaruzzaman M *et al*. Pathogenesis of *Providencia alcalifaciens*-induced diarrhea. *Infect Immun* 1992; **60**: 5017–5024.
5. Guth BEC, Perrella E. Prevalence of invasive ability and other virulence-associated characteristics in *Providencia alcalifaciens* strains isolated in São Paulo, Brazil, *J Med Microbiol* 1996; **45**: 459–462.
6. Haynes J, Hawkey PM. *Providencia alcalifaciens* and travellers' diarrhoea. *BMJ* 1989; **299**: 94–95.
7. Picard B, Picard-Pasquier N, Krishnamoorthy R, Goullet P. Correlation between DNA polymorphism and enzyme polymorphism argues in favour of the delineation of two species within *Providencia alcalifaciens*. *Res Microbiol* 1991; **142**: 965–969.
8. Hickman-Brenner FW, Farmer JJ, Steigerwalt AG, Brenner DJ. *Providencia rustigianii*: a new species in the family Enterobacteriaceae formerly known as *Providencia alcalifaciens* biogroup 3. *J Clin Microbiol* 1983; **17**: 1057–1060.
9. Costas M, Holmes B, Sloss LL. Numerical analysis of electrophoretic protein patterns of *Providencia rustigianii* strains from human diarrhoea and other sources. *J Appl Bacteriol* 1987; **63**: 319–328.
10. Müller HE, O'Hara CM, Fanning GR, Hickman-Brenner FW, Swenson JM, Brenner DJ. *Providencia heimbachae*, a new species of Enterobacteriaceae isolated from animals. *Int J Syst Bacteriol* 1986; **36**: 252–256.
11. Penner JL. The genera *Proteus, Providencia*, and *Morganella*. In: Balows A, Trüper GG, Dworkin M, Harder W, Schleifer KH (eds) The Prokaryotes: a handbook on the biology of bacteria: ecophysiology, isolation, identification, applications. New York, Springer-Verlag. 1992: 2849–2862.
12. Cornaglia G, Frugoni S, Mazzariol A, Piacentini E, Berlusconi A, Fontana R. Activities of oral antibiotics on *Providencia* strains isolated from institutionalized elderly patients with urinary tract infections. *Antimicrob Agents Chemother* 1995; **39**: 2819–2821.
13. Lindsey JO, Martin WT, Sonnenwirth AC, Bennet JV. An outbreak of nosocomial *Proteus rettgeri* urinary tract infection. *Am J Epidemiol* 1976; **103**: 2461–2469.
14. Toni M, Casewell MW, Schito GC. Reappraisal of the significance of multiply resistant urinary isolates of *Proteus rettgeri*. *J Antimicrob Chemother* 1980; **6**: 527–534.
15. Farmer JJ. Enterobacteriaceae: introduction and identification. In: Murray P, Baron E, Pfaller M, Tenover F, Yolken R (eds) Manual of clinical microbiology. Washington, DC, American Society for Microbiology. 1995: 438–449.
16. Rather PN, Orosz E, Shaw KJ, Hare R, Miller G. Characterization and transcriptional regulation of the 2′-N-acetyltransferase gene from *Providencia stuartii*. *J Bacteriol* 1993; **175**: 6492–6498.
17. Gu JW, Neu HC. In vitro activity of Dactimicin, a novel pseudodisaccharide aminoglycoside, compared with activities of other aminoglycosides. *Antimicrob Agents Chemother* 1989; **33**: 1998–2003.
18. Hawkey PM, Penner JL, Linton AH, Hawkey CA, Crisp JL, Hinton M. Speciation, serotyping, antimicrobial sensitivity and plasmid content of Proteeae from the environment of calf-rearing units in South West England. *J Hyg* 1986; **97**: 405–417.