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Emergence of Multidrug-Resistant *Salmonella enterica* Serovar Typhi in Korea

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A chloramphenicol-resistant strain of *Salmonella enterica* serovar Typhi was first noted in Korea in 1992, when a resistant isolate was detected in a returned traveler. Continued isolation of multidrug-resistant (MDR) strains thereafter in other settings prompted a retrospective analysis of laboratory records and phenotypic and genotypic analyses of 12 chloramphenicol-resistant isolates. Among these, one isolate was resistant only to chloramphenicol, and the other isolates were also resistant to ampicillin and co-trimoxazole. MDR was transferred by conjugation from 9 of the 11 isolates. PCR showed that all isolates had an incompatible group HI1 plasmid, and *oriT* was detected in 10 isolates, which included strains with an unsuccessful transfer of resistance. All of the ampicillin-resistant isolates had a β-lactamase band of pI 5.4 and bla_{TEM} alleles. A PCR amplicon from an isolate showed that the sequences were identical to those of bla_{TEM-1}, suggesting that all isolates had a TEM-1 β-lactamase. All isolates had class 1 integrons: 10 isolates had integrons of ca. 1.2 kb with *dhfr7* gene cassettes, and 1 isolate had an integron of ca. 2.3 kb with *aacA4* and bla_{OXA-1}-like gene cassettes. The pulsed-field gel electrophoresis patterns of 7 of 11 MDR isolates were identical and indistinguishable from those reported for isolates in India and Indonesia. In conclusion, some of the MDR strains in Korea are related to those in other Asian countries. Susceptibility testing became necessary for selection of antimicrobial agents for the optimal treatment of patients with the emergence of MDR *Salmonella* serovar Typhi in Korea.

Typhoid fever, a systemic infectious disease caused by *Salmonella enterica* serovar Typhi, affected an estimated 16 million people in the 1990s, with 600,000 deaths reported annually worldwide (10). It has become a rare imported disease in developed countries (9), but massive outbreaks still occur in some countries, as was shown in Tajikistan due to the consumption of contaminated municipal water (17). The rate of typhoid fever in Korea has decreased markedly over the last decade, but sporadic cases and small outbreaks still occur.

Antimicrobial therapy is generally not required for the treatment of gastrointestinal infections caused by nontyphoidal *Salmonella* strains. However, effective antimicrobial therapy is required for typhoid fever to reduce morbidity and mortality (18). Historically, the drugs of choice were chloramphenicol, ampicillin, and trimethoprim-sulfamethoxazole (co-trimoxazole). However, antimicrobial-resistant *Salmonella* serovar Typhi isolates emerged in the 1970s in Latin America (21) and Asia (3). A large number of *Salmonella* serovar Typhi strains have been isolated in Korea, but no resistant strain was documented until 1992, when a chloramphenicol-, ampicillin-, and co-trimoxazole-resistant strain was isolated from a patient who returned from a Southeast Asian country (K. Lee, D. Yong, J. H. Yum, Y. S. Lim, Y. Chong, and B.-K. Lee, Abstr. 43rd Intersci. Conf. Antimicrob. Agents Chemother., abstr. C2-865, 2003). We isolated two additional multidrug-resistant (MDR) strains in 1995, and subsequently, Shin et al. (27) reported a chloramphenicol resistance rate of 15% among isolates in Korea in 1997.

MDR *Salmonella* serovar Typhi isolates commonly harbor a plasmid of incompatibility group HI1. A 365-bp region of the RepHI1A region was detected in MDR strains of *Salmonella* serovar Typhi isolated in India (26). *oriT* is located within the Tra1 region of the plasmid and contains the *nic* site, which is one of many genes required for conjugative transfer of IncHI1 plasmid (12). The emergence of MDR *Salmonella* serovar Typhi in Korea was possibly due to the acquisition of the resistance by endemic strains from other resistant gram-negative bacilli or to the spread of resistant strains from other countries to which there had been recent increases in international travel. To verify these assumptions, comparisons of the phenotypic and genotypic characteristics of both our susceptible and our resistant isolates are required.

The aims of this study were to analyze retrospectively the trends in the isolation and susceptibilities of *Salmonella* serovar Typhi strains from stool specimens at a Korean hospital and to determine the phenotypic and genotypic characteristics of recent isolates of chloramphenicol-resistant *Salmonella* serovar Typhi strains, including the first three strains isolated.

MATERIALS AND METHODS

Isolation and antimicrobial susceptibility trends for *Salmonella* serovar Typhi. Stool culture data obtained from 1969 to 1998 at a medical college-affiliated hospital in Seoul, Korea, were used for retrospective analysis. During that period, the methods of isolation and identification of *Salmonella* serovar Typhi remained essentially similar and were based on conventional methods, including the use of selenite broth, MacConkey agar, and salmonella-shigella agar for isolation and the use of triple sugar iron agar and other biochemical tests (6). The O-group antigen was determined by the slide agglutination method with commercial antisera (Difco, Detroit, Mich.) or antisera produced by the National

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TABLE 1. Trends in isolation of enteric pathogens from stool specimens at a medical college-affiliated hospital in Seoul and antimicrobial susceptibilities of *Salmonella* serovar Typhi isolates

Enteric pathogen	No. (%) of isolates by year[a]				
	1969–1978	1979–1988	1989–1993	1994–1998	Total
Salmonella serovar Typhi	472 (21.8)	469 (12.5)	44 (6.5)	14 (1.5)	999 (13.3)
Salmonella serovar Paratyphi A	18 (0.8)	101 (2.7)	2 (0.3)	1 (0.1)	122 (1.6)
Other *Salmonella* serovars	504 (23.3)	1,102 (29.4)	436 (63.9)	735 (78.4)	2,777 (36.8)
Shigella spp.	1,039 (47.9)	1,508 (40.2)	37 (5.4)	14 (1.5)	2,598 (34.5)
Yersinia enterocolitica	NT[b]	29 (0.8)	9 (1.3)	9 (1.0)	47 (0.6)
Campylobacter spp.	NT	185 (4.9)	101 (14.8)	138 (14.7)	424 (5.6)
Vibrio parahaemolyticus	45 (2.1)	96 (2.6)	20 (2.9)	22 (2.3)	183 (2.4)
Others[c]	89 (4.1)	262 (7.0)	33 (4.8)	5 (0.5)	389 (5.2)
Total	2,167 (100)	3,752 (100)	682 (100)	938 (100)	7,539 (100)

[a] All isolates recovered from 1969 to 1978 were susceptible to ampicillin and chloramphenicol (the isolates were not tested for their co-trimoxazole susceptibilities). All isolates recovered from 1979 to 1993 were susceptible to ampicillin, chloramphenicol, and co-trimoxazole. Two of 14 (12.8%) isolates recovered from 1994 to 1998 were resistant to the three drugs. The first multidrug-resistant isolate at another hospital, in 1992 which was detected was not included.

[b] NT, not tested.

[c] Enteropathogenic *E. coli* and *Plesiomonas shigelloides*.

Institute of Health of Korea (NIHK). Antimicrobial susceptibility was determined with commercial disks (Difco or Becton Dickinson, Cockeysville, Md.) by the Kirby-Bauer disk diffusion method (2) until the NCCLS method replaced it in 1978 (20).

Antimicrobial susceptibilities of recent isolates. Strains isolated from 1992 to 1998 were used for the characterization of chloramphenicol-resistant *Salmonella* serovar Typhi: three strains were isolated at two hospitals affiliated with a medical college in Seoul, and nine strains were isolated by NIHK. Chloramphenicol-susceptible isolates (9 and 13 strains isolated in 1989 and 1998, respectively) were used for comparison. Antimicrobial susceptibility was tested by the agar dilution method (20). The antimicrobial agents used were ampicillin, cephalothin, tetracycline, and nalidixic acid (Sigma Chemical, St. Louis, Mo.); cefotaxime (Aventis, Frankfurt, Germany); cefoxitin (Merck Sharp & Dohme, Rahway, N.J.); sulbactam (Pfizer Korea, Seoul, Korea); chloramphenicol (Chong Kun Dang, Seoul, Korea); sulfamethoxazole and trimethoprim (Dong Wha Pharmaceutical, Seoul, Korea); and ciprofloxacin (Bayer Korea, Seoul, Korea). *Escherichia coli* strain ATCC 25922 was used for quality control.

Conjugation and plasmid preparation. Resistance transfer was tested by an agar mating method with nalidixic acid-resistant recipient *E. coli* RG 176. The plasmid was isolated by the alkaline lysis method (25), and the plasmid size was estimated by comparing it to those of plasmids from *E. coli* strain V517 and *Klebsiella pneumoniae* ATCC 700603.

PCR. DNAs were extracted by boiling whole cells and were used as templates. The alleles for bla_{TEM} and the class 1 integron were detected by methods reported previously (4, 13). A 365-bp region of the RepHI1A replicon was amplified by PCR, which was based on previous studies (7, 26), with primer HI1A-F (5′-GGT CCA ACC CAT TGC TTT AC-3′) and primer HI1A-R (5′-CAC GGA AAG AAA TCA CAA C-3′). A 285-bp *oriT* region was detected with primer F (5′-ATA TGG TAC CGG TTA TTG CTA CTT AAT GCC GA-3′) and primer R (5′-ATA TAA GCT TAT CTG ATT CTG ACA TGT GCG-3′) (12). *E. coli* strains YMC IEF-1 and ATCC 25922 were used as TEM-1-positive and -negative controls, respectively.

Isoelectric focusing. Bacterial cells were broken by sonication, and the supernatant was used to determine the isoelectric points of the β-lactamases (16). Electrophoresis was performed with a commercial gel (pI 3 to 10) and a temperature control system (Novel Experimental Technology, San Diego, Calif.). After electrophoresis, the gel was overlaid with filter paper that had been soaked in a nitrocefin solution of 0.7 mg/ml. Sonicates of the following control strains, obtained from A. Bauernfeind (Munich, Germany), were used to determine the pIs: *E. coli* YMC IEF-1 (TEM-1, pI 5.4), YMC IEF-3 (TEM-52, pI 6.0), and Cho-TC (CMY-1, pI 8.0) and *K. pneumoniae* YMC IEF-4 (SHV-3, pI 7.0) and YMC IEF-5 (SHV-2, pI 7.6).

Nucleotide sequencing. PCR products were used to analyze the nucleotide sequences of bla_{TEM} in YMC 95/6/4405S and bla_{OXA}-containing class 1 integrons in YMC 95/6/4405S and YMC 98/P110N. After electrophoresis of the PCR products, the DNA was extracted with a gel extraction kit (Qiagen, Hilden, Germany) and was used for direct sequencing. Both strands were analyzed by the dideoxy-chain termination method with an ABI 3700 autosequencer (Perkin-Elmer, Foster City, Calif.).

Pulsed-field gel electrophoresis (PFGE). Agarose-embedded chromosomal DNAs of *Salmonella* serovar Typhi were prepared according to the instructions of the instrument manufacturer (Bio-Rad, Hercules, Calif.). The DNA was digested with XbaI, and the bands were separated with a CHEF-DR II system (Bio-Rad). The electrophoresis conditions were as follows: switch times, an initial 0.5 s and a final 30 s; field strength, 6 V; and run time, 20 h. After electrophoresis, the gel was stained with ethidium bromide and the band patterns were compared both visually and by using Uniband/MAP software (UVItec Ltd., Cambridge, United Kingdom). The confidence level was set at 2% to show a similarity of 1.0 for two lanes with visually identical patterns and a similarity of approximately 0.9 for possibly related patterns (a six-fragment difference), as recommended by Tenover et al. (28).

Nucleotide sequence accession numbers. The nucleotide sequences reported in this work have been assigned to the GenBank database under accession numbers AY245101 (the *dhfr7*-carrying class 1 integron) and AY348316 (*aacA4* and bla_{OXA-1}-like gene carrying the class 1 integron).

RESULTS

Typhoid fever used to be a highly endemic disease in Korea. The mean annual number of *Salmonella* serovar Typhi isolates recovered from stool specimens from 1969 to 1988 at a medical college-affiliated hospital was more than 40 (Table 1). In the following two 5-year periods, the mean number of isolates recovered annually decreased to 8.8 and 2.8, respectively. During the period from 1974 to 1983 at the same hospital, the annual mean numbers of patients harboring *Salmonella* serovar Typhi and *S. enterica* serovar Paratyphi A, as determined from blood cultures, were 217 and 61, respectively (17.2 and 4.8% of all culture-positive patients, respectively). In 1991, the number of patients at the same hospital whose blood harbored *Salmonella* serovar Typhi was 22 (0.6% of culture-positive patients); and this number then decreased further, but the organism was still occasionally isolated (data not shown).

Isolation of the first MDR *Salmonella* serovar Typhi strain in 1992 at one of two hospitals affiliated with a medical college, from a patient who had returned from a Southeast Asian country, prompted an analysis of the records. However, among the 985 strains isolated from 1969 to 1993 at the main hospital of the same medical college, none were resistant to chloramphenicol, ampicillin, or co-trimoxazole. In 1995, we isolated two more MDR strains from a 52-year-old male patient and a

TABLE 2. Comparison of susceptibilities of chloramphenicol-susceptible and -resistant *Salmonella* serovar Typhi isolates

Isolate type (yr isolated)[a]	Antimicrobial agent	MIC (μg/ml)[b]			Susceptibility (%)[c]		
		Range	50%	90%	S	I	R
Chloramphenicol resistant (1992–1998; $n = 12$)	Ampicillin	4–>128	>128	>128	8	0	92
	Ampicillin-sulbactam	4–32	32	32	8	0	92
	Cephalothin	8–16	8	16	56	44	0
	Chloramphenicol	32–>128	>128	>128	0	0	100
	Co-trimoxazole	0.12/2.28–128/2,432	128/2,432	128/2,432	8	0	92
	Tetracycline	2–>128	>128	>128	8	0	92
Chloramphenicol susceptible (1989–1998; $n = 21$)	Ampicillin	0.5–1	0.5	1	100	0	0
	Ampicillin-sulbactam	0.5–1	0.5	1	100	0	0
	Cephalothin	2–8	2	2	100	0	0
	Chloramphenicol	4–8	4	4	100	0	0
	Co-trimoxazole	0.06/1.14–0.12/2.28	0.06/1.14	0.06/1.14	100	0	0
	Tetracycline	1	1	1	100	0	0

[a] Therapeutically nonrelevant drugs were also included to compare the antibiograms of chloramphenicol-susceptible and -resistant isolates. All of the isolates were inhibited by ≤0.12 μg of cefotaxime per ml, ≤0.015 μg of ciprofloxacin per ml, and ≤8 μg of nalidixic acid per ml.
[b] 50% and 90%, MICs at which 50 and 90% of isolates, respectively, are inhibited.
[c] Abbreviations: S, susceptible, I, intermediate; R, resistant.

59-year-old female patient with no history of overseas travel (Table 1).

The antimicrobial susceptibilities of chloramphenicol-resistant and -susceptible recent clinical isolates were compared. Among the 12 chloramphenicol-resistant *Salmonella* serovar Typhi strains isolated from 1992 to 1998, 11 also showed resistance to ampicillin and co-trimoxazole (Table 2). The ranges of MICs of nalidixic acid and ciprofloxacin were 4 to 8 and ≤0.015 μg/ml, respectively, for both chloramphenicol-resistant and -susceptible isolates.

Eleven MDR isolates were tested to determine their characteristics (Table 3). The MDR was transferred en bloc by conjugation from 9 of 11 isolates to an *E. coli* recipient. The conjugative plasmid had a size of ca. 120 MDa. The first MDR isolate in Korea (strain 1) and another isolate (strain 9) also had plasmids of similar sizes, but repeated attempts to transfer the resistance even at 28°C were unsuccessful.

PCR was used to determine the incompatibility group of the plasmid. A 365-bp region of the RepHI1 A replicon was detected in all 11 isolates, including 2 conjugation-negative isolates. The *oriT* allele was detected in all isolates except one (strain 11).

bla_{TEM} alleles were detected in all of the ampicillin-resistant isolates, and the isolates had bands for a β-lactamase of pI 5.4. A PCR amplicon from an isolate (strain 2) had sequences identical to those of bla_{TEM-1}. This suggests that all isolates had the TEM-1 β-lactamase. In our study, class 1 integrons were detected by PCR in all 11 MDR isolates. They were ca. 1.2 kb in 10 isolates and ca. 2.3 kb in 1 isolate. Sequencing of the 1.2-kb integron from one isolate (strain 2) showed carriage of a *dhfr7* gene cassette (Fig. 1A). The strain carrying a 2.3-kb integron had a β-lactamase band of ca. pI 7.4. Sequencing showed that the integron carried *aacA4*, bla_{OXA-1}-like resistance gene cassettes, and a short unknown open reading frame (Fig. 1B).

The PFGE patterns of XbaI-digested genomic DNA of 12 and 19 chloramphenicol-resistant and -susceptible *Salmonella* serovar Typhi isolates, respectively, were compared. The pattern of the first MDR isolate in Korea (type A) was different from those of the other MDR isolates. The remaining 10 MDR

TABLE 3. Characteristics of MDR *Salmonella* serovar Typhi isolates

YMC strain (no.) name	Conjugation result	PCR result for:				β-Lactamase pI	PFGE type
		oriT	IncHII[a]	Integron[b]	bla_{TEM}		
(1) 92/8/5479Y	−	+	+	1.2	+	5.4	A
(2) 95/6/4405S	+	+	+	1.2[c]	+[c]	5.4	C
(3) 95/12/4248S	+	+	+	1.2	+	5.4	D
(4) 98/K101N	+	+	+	1.2	+	5.4	E
(5) 98/O102N	+	+	+	1.2	+	5.4	C
(6) 98/H103N	+	+	+	1.2	+	5.4	C
(7) 98/H104N	+	+	+	1.2	+	5.4	C
(8) 98/H105N	+	+	+	1.2	+	5.4	C
(9) 98/Y106N	−	+	+	1.2	+	5.4	C
(10) 98/S109N	+	+	+	1.2	+	5.4	C
(11) 98/P110N	+	−	+	2.3[c]	+	5.4, ~7.4	C

[a] A 365-bp region of the RepHI1A replicon.
[b] Class 1 integron. Data represent approximate sizes (in kilobases).
[c] The nucleotides of integrons and bla_{TEM-1} were sequenced.

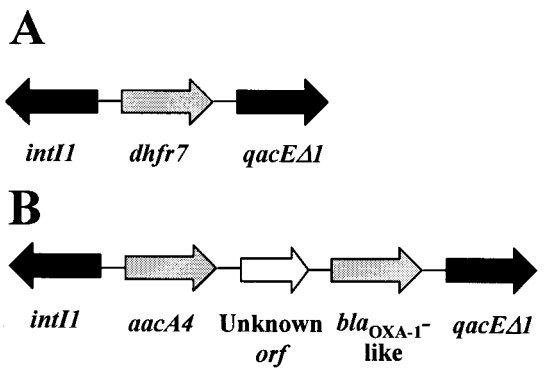

FIG. 1. Schematic structures of class 1 integrons in multidrug-resistant *Salmonella* serovar Typhi isolates. (A) The integron in strain YMC 95/6/4405S contained only one resistance gene cassette, *dhfr7* (GenBank accession no. AY245101). (B) The integron in strain YMC 98/P110N contained two resistance gene cassettes, *aacA4* and a bla_{OXA-1}-like cassette (GenBank accession no. AY348316).

isolates clustered together: the second MDR strain, isolated in 1995 (Fig. 2, lane 3, type C), showed a pattern identical to those of the seven NIHK strains isolated in 1998 (Fig. 2, lane 6).

One strain that was isolated in 1998 and that was resistant only to chloramphenicol (type M) clustered together with susceptible strains isolated in 1989 (types K, L, N, O, and P). All nine antimicrobial-susceptible strains isolated in 1998 clustered together (types F to I).

DISCUSSION

Until the 1980s typhoid fever was an endemic disease in Korea and *Salmonella* serovar Typhi was frequently isolated from stool specimens (Table 1). Typhoid fever is a serious systemic infection requiring proper antimicrobial therapy. The present retrospective analysis showed that antimicrobial-resistant *Salmonella* serovar Typhi was absent until 1992, when it was detected in a hospital in Korea (Lee et al., 43rd ICAAC), although MDR *Salmonella* serovar Typhi became prevalent in Southeast Asia (8, 30), the Middle East, and northeastern Africa (1, 19, 23).

Among the chloramphenicol-resistant *Salmonella* serovar Typhi strains isolated in the 1990s, 1 chloramphenicol-resistant isolate was susceptible to ampicillin and co-trimoxazole, but the remaining 11 were also resistant to ampicillin and co-trimoxazole (Table 2). Some of the chloramphenicol-resistant isolates were either intermediate or resistant to cephalothin or tetracycline (Table 2), but all 11 MDR isolates were susceptible to ciprofloxacin and nalidixic acid. Ciprofloxacin is recommended as the drug of choice for the treatment of multidrug-resistant *Salmonella* serovar Typhi infections (18). However, an NIHK study suggested that the clinical failure of empirical fluoroquinolone treatment might occur, as the nalidixic acid resistance rate rapidly increased from 3.5% in 2001 to 23.3% in 2002, with resistance detected in 138 and 58 isolates, respectively (data not shown). Low-level fluoroquinolone resistance can be detected by testing only for nalidixic acid resistance (5). It is a concern that ceftriaxone remains the only drug of choice for the treatment of infections due to ampicillin- and fluoroquinolone-resistant isolates.

It was reported that most MDR *Salmonella* serovar Typhi isolates have a conjugative plasmid of the IncHI1 type. This plasmid has been implicated as a significant factor in the persistence and reemergence of *Salmonella* serovar Typhi (11, 19). The reported sizes of the plasmids were quite variable: 220 and 290 kb in isolates from Bangladesh (8); 91.2 MDa in isolates from Tehran, Iran (1); and 110 to 120 MDa in isolates from India (30). The type of β-lactamase reported was mostly TEM-1. Most of our MDR strains also had similar characteristics: they had a ca. 120-MDa conjugative plasmids of the IncHI1 type, they transferred MDR en bloc, and they had the TEM-1 β-lactamase. However, a few of our isolates showed heterogeneity. Repeated attempts to transfer the resistance by conjugation from the first chloramphenicol-resistant strain isolated in Korea (strain 1 in Table 3) failed, even at 28°C; one isolate was PCR negative for the *oriT* allele.

Integrons are a major vehicle for the spread of multiple-antibiotic resistance (14). Class 1 integrons were detected in all 11 MDR isolates. Their sizes were ca. 1.2 kb in all except one isolate, in which it was ca. 2.3 kb. The smaller integron contained only a *dhfr7* resistance gene cassette, but the larger one contained *aacA4* and bla_{OXA-1}-like gene cassettes (Fig. 1). Ploy et al. (24) reported that all 18 of their resistant *Salmonella* serovar Typhi isolates had class 1 integrons with *dfrVII* gene cassettes. Pai et al. (22) reported that an MDR strain isolated in Korea in 1999 had a class 1 integron with the *aacA4b*, *catB8*, *aadA1*, *dfrA1*, and *aac(6′)-IIa* gene cassettes and a novel *blaP2* cassette. *blaP2* is a carbenicillinase gene. These results obtained from studies performed in Korea indicate the existence of various β-lactamase genes in ampicillin-resistant *Salmonella* serovar Typhi isolates.

In a comparison of various molecular characteristics, Ling et al. (15) reported that isolates obtained in Hong Kong in 1985 to 1997 differed from those obtained in Vietnam in 1989 and 1990. They reported that 37% of the Vietnamese isolates belonged to two predominant clones. It was reported that the PFGE pattern of XbaI-digested genomic DNA of *Salmonella* serovar Typhi was stable (29). Interestingly, 7 of our 11 MDR isolates had identical PFGE patterns (Fig. 2, type C), and that pattern was also apparently identical to that of the MDR strains isolated in 1993 and 1994 in India (Fig. 2, lanes 7, 8, and 10, in reference 26) and to that of 1 of 5 Indonesian isolates recovered in 1992 and 1994 (Fig. 1A, lane 14, in reference 29). These results indicate that our MDR strains are related to those in other countries. Ispahani and Slack (9) reported that from 1980 to 1997 all 21 typhoid fever patients at a hospital in the United Kingdom were of Asian descent, and some had a history of travel to Asia. Some of these isolates were MDR strains. With increasing international travel, the further spread of MDR strains can be anticipated. Seven of our eight MDR strains with identical PFGE types were isolated from patients in five cities in one province, suggesting clonal spread. Routine antimicrobial susceptibility testing of *Salmonella* serovar Typhi isolates became crucial for the optimal treatment of typhoid fever patients in Korea.

In conclusion, the characteristics of chloramphenicol-resistant strains isolated in Korea from 1992 to 1998 were mostly similar to those reported for isolates in other countries: they

PFGE type (No. of isolates)	Susceptibility	Representative isolate
M		Marker
A (1)	MDR	92/8/5479Y
B (1)	S	89/10/5766
C (1)	MDR	95/6/4405
C (7)	MDR	98/O102N
D (1)	MDR	95/12/4248
E (1)	MDR	98/K101N
F (6)	S	98/4/7371
G (1)	S	98/5/5294
H (1)	S	98/5/7377
I (1)	S	98/8/6472
J (1)	S	89/2/5105
K (1)	S	89/9/4204
L (1)	S	89/10/6282
M (1)	CHL R	98/P348N
N (1)	S	89/11/4225
O (2)	S	89/8/5369
P (1)	S	89/7/5439
Q (1)	S	89/6/5177
R (1)	S	89/2/2127

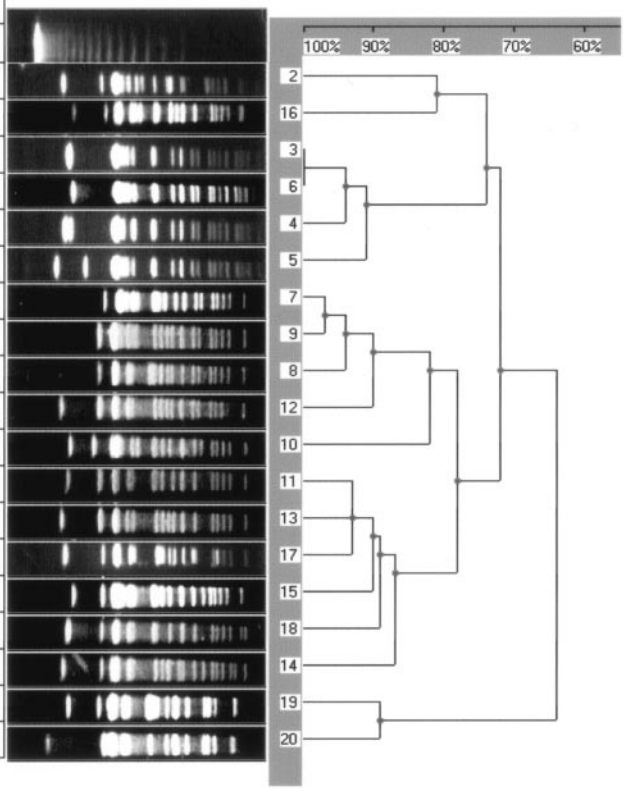

FIG. 2. PFGE patterns of XbaI-digested genomic DNA of 11 MDR isolates, 1 chloramphenicol-resistant isolate, and 14 antimicrobial-susceptible isolates of *Salmonella* serovar Typhi. The pattern of the first MDR strain, which was isolated in 1992 (type A), was different from those of the remaining 10 MDR strains, which were isolated from 1995 to 1998 and which clustered together (types C to E). One strain (type M), which was isolated in 1998 and which was resistant only to chloramphenicol, clustered together with six susceptible strains (types K, L, N, O, and P) isolated in 1989. All nine antimicrobial-susceptible strains isolated in 1998 clustered together (types F to I).

were MDR, carried large conjugative IncHI1 plasmids, had the TEM-1 β-lactamase, and had class 1 integrons. Some strains had subtle differences in characteristics: the nontransferability of resistance or an integron with a bla_{OXA} gene cassette. With the emergence of MDR *Salmonella* serovar Typhi in Korea, susceptibility testing became necessary for selection of the antimicrobial agents that could be used for the optimal treatment of patients.

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