

Antimicrobial resistance among salmonella isolates from hospitals in Rome

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SUMMARY

The susceptibility to antimicrobial agents of 569 salmonella isolates collected in 1977–8 from patients in hospitals in Rome was tested. Fifty-nine per cent of all isolates were resistant to one or more antimicrobials. Resistance was most common to sulphathiazole, tetracycline, streptomycin, whereas colistin, gentamicin, tobramycin, trimethoprim-sulphamethoxazole and nalidixic acid were the most active *in vitro*.

Multiple resistance was most frequently found in strains of *Salmonella wien* and *S. typhimurium* (94% and 38% respectively).

A significant change in the resistance pattern of *S. wien* was observed between 1977 and 1978, with a significant increase of susceptibility to some antimicrobials in 1978.

Twenty-one R-plasmids transmissible to *E. coli* K12 were derived from 46 resistant strains of *S. typhimurium*.

INTRODUCTION

Antimicrobial drug resistance is a major public health problem; therefore, a surveillance system to control and possibly prevent this phenomenon is extremely important (O.M.S. 1978).

Particular interest has focused on the genus *Salmonella*, and the antimicrobial resistance pattern and presence of R-plasmids in these bacteria have been studied (Anderson & Lewis, 1965; Schroeder, Terry & Bennett, 1968; Winshell *et al.* 1970; Pocurull, Gaines & Mercer, 1971; Marks, Kazemi & McKay, 1973; Bissett, Abbott & Wood, 1974; Neu *et al.* 1975; Voogd *et al.* 1973, 1977; Duck *et al.* 1978).

In this paper, the antimicrobial susceptibility of 569 salmonella isolates, collected during 1977–78 from 22 hospitals in Rome is examined.

MATERIALS AND METHODS

Bacterial strains

Salmonella strains were isolated from patients in 22 hospitals in Rome from January 1977 to December 1978 and sent to the Centro Nazionale per gli Enterobatteri Patogeni of the Istituto Superiore di Sanità for typing.

All strains were identified by common biochemical and serological tests (Kauffmann, 1966; Edwards & Ewing, 1973).

For antibiotic susceptibility testing a control strain of *Escherichia coli* ATCC 25922 was used. In the conjugation procedure, two strains of *E. coli* K 12 were used as receptors (kindly provided by Professor E. Romero, Istituto di Microbiologia dell'Università di Pavia, Italy); one was a nalidixic acid-resistant mutant J53 (pro⁻, met⁻, Nx^R) and the other was a rifampicin-resistant mutant 309 (cis⁻, his⁻, Hfr, Rif^R).

Antibiotic susceptibility testing

The method described by Bauer *et al.* (1966) and further defined by the N.C.C.L.S. (1975) was used. The following antibiotic discs (BBL) were used: nalidixic acid (Nx), 30 µg; cephalothin (Ce), 30 µg; chloramphenicol (C), 30 µg; colistin (Cl), 10 µg; gentamicin (G), 10 µg; kanamycin (K), 30 µg; trimethoprim-sulphamethoxazole (Tm), 1.25 µg and 23.75 µg; streptomycin (S), 10 µg; tetracycline (T), 30 µg; tobramycin (To), 10 µg; sulphathiazole (Su), 1.0 mg; ampicillin (A), 10 µg.

Iso-sensitest broth (Oxoid) was used for all liquid cultures and iso-sensitest agar (Oxoid) was used for antibiotic susceptibility testing.

Conjugation procedure

R-plasmid transfer from wild strains to *E. coli* K 12 was performed as described by Datta & Hedges (1972).

Data analysis

Statistical data were analysed with the BMDP statistical package from UCLA (Dixon, 1975) using an IBM 370 of the Computer Center of the Istituto Superiore di Sanità. Statistical differences were analysed using the χ^2 test with continuous Yates correction (Armitage, 1975).

RESULTS

Table 1 shows the distribution of the serotypes of the 569 salmonella strains studied. Fifty-nine per cent of strains were resistant to one or more antimicrobial agents; the overall prevalence of antimicrobial resistance was 98% in *S. wien*, 61% in *S. typhimurium*, 56% in *S. panama*, 36% in *S. livingstone*, 29% in *S. enteritidis*, 0% in *S. typhi*, and 51% in all other serotypes.

Table 2 shows the number of resistance determinants found in the seven most frequent serotypes; most of the strains were sensitive to all antimicrobial agents

Table 1. *Salmonella* serotypes isolated in 22 hospitals in Rome in 1977-8

Serotype	1977		1978		1977-8	
	No. of strains	%	No. of strains	%	No. of strains	%
<i>S. wien</i>	96	28.6	36	15.4	132	23.2
<i>S. typhimurium</i> *	81	24.2	42	17.9	123	21.6
<i>S. enteritidis</i>	23	6.9	25	10.7	48	8.4
<i>S. typhi</i>	18	5.4	21	9.0	39	6.9
<i>S. panama</i>	21	6.3	16	6.8	37	6.5
<i>S. livingstone</i>	13	3.9	9	3.8	22	3.9
<i>S. infantis</i>	7	2.1	11	4.7	18	3.2
<i>S. london</i>	9	2.7	6	2.6	15	2.6
<i>S. anatum</i>	7	2.1	6	2.6	13	2.3
<i>S. manhattan</i>	5	1.5	7	3.0	12	2.1
<i>S. newport</i>	1	0.3	10	4.3	11	1.9
<i>S. heidelberg</i>	4	1.2	6	2.6	10	1.8
Others	50	14.9	3.9	16.7	89	15.6
Total number of strains	335	100	234	100	569	100

* This includes *S. typhimurium* var. *copenhagen*.

tested (232, 40 %); 124 (21 %) were resistant to one and the remaining 213 (37 %) were resistant to two or more. *S. typhi* showed no resistance, and no isolate of *S. livingstone* was resistant to more than two antimicrobials. *S. wien* was clearly the serotype with the highest percentage of multiply-resistant strains (94 %) followed by *S. typhimurium* (38 %), *S. panama* (16 %) and *S. enteritidis* (10 %); taken together the isolates of other serotypes had an 18 % prevalence rate of multiply-resistant strains.

Table 3 shows the prevalence rates of resistance to individual antimicrobial agents by serotype. Resistance to sulphathiazole was the most common one, followed by resistance to tetracycline and streptomycin. Resistance was also common with ampicillin, chloramphenicol, kanamycin and cephalothin. Sensitivity was most common with colistin, nalidixic acid, gentamicin, tobramycin and trimethoprim-sulphamethoxazole, which were active enough against *S. wien* as well. In 1977, resistance to gentamicin and tobramycin was limited to *S. wien* isolates, whereas in 1978 a strain of *S. panama* and one of *S. heidelberg* were identified to be resistant to gentamicin. *S. typhimurium* showed a number of tetracycline- and streptomycin-resistant strains significantly higher than other serotypes ($P < 10^{-5}$), excluding *S. wien*; isolates of *S. panama* were particularly resistant to sulphathiazole.

Table 4 and table 5 show the difference in antibiotic resistance between strains isolated in 1977 and 1978; in 1978 the pattern of resistance of *S. wien* was characterized by a significant fall in the number of the strains which were resistant to ampicillin, sulphathiazole, tetracycline, streptomycin, kanamycin, chloramphenicol, cephalothin and nalidixic acid ($P \leq 0.05$). Moreover an increased resistance to gentamicin, tobramycin and trimethoprim-sulphamethoxazole was observed, although it was statistically not significant.

A significant increase of resistance to streptomycin and sulphathiazole was found

Table 2. Multiple antimicrobial resistance in salmonella serotypes

Serotype	No. of resistances ^a											No. of strains tested	
	0	1	2	3	4	5	6	7	8	9	10		11
<i>S. wien</i>	1.5	3.8	2.5	2.3	12.9	3.8	7.6	42.4	13.6	7.5	1.5	0.8	132
<i>S. typhimurium</i> ^b	36.6	25.2	21.1	6.5	4.9	2.4	1.6	1.6	—	—	—	—	123
<i>S. enteritidis</i>	70.8	18.7	2.1	—	4.2	—	2.1	2.1	—	—	—	—	48
<i>S. typhi</i>	100	—	—	—	—	—	—	—	—	—	—	—	39
<i>S. panama</i>	43.2	40.6	2.7	5.4	—	2.7	2.7	—	—	2.7	—	—	37
<i>S. livingstone</i>	63.6	31.8	4.6	—	—	—	—	—	—	—	—	—	22
<i>S. infantis</i>	66.7	22.3	5.5	—	—	—	5.5	—	—	—	—	—	18
Others	46.7	35.3	10.0	4.0	2.0	—	1.3	—	0.6	—	—	—	150
Total no. strains	232	124	48	19	28	9	17	59	19	11	2	1	569

^a Values expressed as percentage of total number of isolates for each serotype.

^b This includes *S. typhimurium* var. *copenhagen*.

Table 3. Resistance of salmonella strains isolated in 1977-8 to individual agents, by serotype

Serotype	No. of strains tested	Antimicrobial agent ^a													Total
		Nx	Ce	C	Cl	Tm	G	K	S	T	To	Su	A		
<i>S. wien</i>	132	11.4 ^b	74.8	73.3	5.3	13.6	14.4	81.8	81.1	76.5	14.4	83.3	82.3	98.5	
<i>S. typhimurium</i> ^c	123	0	4.1	8.1	0.8	2.4	0	7.3	31.7	38.2	0	38.2	13.0	63.4	
<i>S. enteritidis</i>	48	0	2.1	8.3	0	2.1	0	4.2	10.4	10.4	0	29.2	0.3	29.2	
<i>S. typhi</i>	39	0	0	0	0	0	0	0	0	0	0	0	0	0	
<i>S. panama</i>	37	2.7	2.7	8.1	5.4	0	2.7	5.4	13.5	16.2	0	51.4	8.3	56.7	
<i>S. livingstone</i>	22	0	0	0	0	4.5	0	0	0	0	0	36.4	0	36.4	
Others	168	1.2	1.8	3.0	1.2	4.2	0.6	4.8	11.9	11.3	0	38.7	5.4	51.2	
All serotypes	569	3.2	19.0	23.2	2.1	5.3	3.7	22.7	30.9	31.3	3.3	46.2	26.0	59.2	

^a Abbreviations as in Materials and Methods.

^b Data are given as percentages of resistant strains.

^c This includes *S. typhimurium* var. *copenhagen*.

Table 4. Resistance of salmonella strains isolated in 1977 to individual antimicrobial agents, by serotype

Serotype	No. of strains tested	Antimicrobial agent ^a											
		Nx	Ce	C	Cl	Tm	G	K	S	T	To	Su	A
<i>S. wien</i>	96	14.6 ^b	83.3	90.6	6.3	12.5	12.5	89.6	88.5	86.5	11.5	89.6	96.8
<i>S. typhimurium</i> ^c	81	0	4.9	7.4	1.2	1.2	0	9.8	25.9	35.8	0	32.0	16.0
Others	158	0	1.2	2.5	0	0.6	0	4.4	6.3	8.8	0	25.3	2.5

^a Abbreviations as in Materials and Methods.

^b Data are given as percentages of resistant strains.

^c This includes *S. typhimurium* var. *coopenhagen*.

Table 5. Resistance of salmonella strains isolated in 1978 to individual antimicrobial agents, by serotype

Serotype	No. of strains tested	Antimicrobial agent ^a											
		Nx	Ce	C	Cl	Tm	G	K	S	T	To	Su	A
<i>S. wien</i>	36	2.8 ^b	50.0	63.9	2.8	16.7	19.4	61.1	61.1	50.0	22.2	66.7	69.4
<i>S. typhimurium</i> ^c	42	0	2.3	9.5	0	4.7	0	2.3	42.8	42.8	0	50.0	7.1
Others	156	1.9	1.9	5.1	2.6	5.1	1.3	3.2	12.8	10.3	0	42.9	7.1

^a Abbreviations as in Materials and Methods.

^b Data are given as percentages of resistant strains.

^c This includes *S. typhimurium* var. *coopenhagen*.

Table 6. *Resistance patterns of S. wien strains isolated in 1977-8*

Resistance patterns*	1977		1978		1977-8	
	No. of strains	%	No. of strains	%	No. of strains	%
Sensitive	—	—	2	5.6	2	1.5
ACCeKSSuT	45	46.9	5	13.9	50	37.9
ACKT	6	6.3	7	19.4	13	9.8
ACCeGKSuTo	7	7.3	3	8.3	10	7.6
ACCeKNxSSuTTm	7	7.3	—	—	7	5.3
Su	—	—	4	11.1	4	3.0
ACeSSuT	3	3.1	—	—	3	2.3
ACCeKNxSSuT	3	3.1	—	—	3	2.3
ACKSSuT	3	3.1	—	—	3	2.3
ACeSSu	1	1.0	1	2.8	2	1.5
ACGKSSuTo	2	2.1	—	—	2	1.5
ACCeKSSuTTm	2	2.1	1	2.8	3	2.3
ACCeGKSSuTmTo	—	—	2	5.6	2	1.5
ACCeSSuT	2	2.1	—	—	2	1.5
Other 26 patterns	15	15.6	11	30.5	26	19.7
Total	96	100	36	100	132	100

* Abbreviations as in Materials and Methods.

in 1978 in strains of *S. typhimurium* ($P \leq 0.05$); besides a significant increase of resistance to ampicillin, sulphathiazole and streptomycin was observed in the other serotypes ($P \leq 0.05$).

Table 6 and table 7 show the patterns of resistance of the most frequent serotypes. The patterns of *S. wien* are separately reported (Table 6) because of their extent.

The most frequent pattern was ACCeKSSuT, the other ones were less frequent. The spread of patterns of resistance, which has been observed among strains isolated in 1978, supports the hypothesis that *S. wien* resistance may be changing in time (Fig. 1).

Table 7 shows the patterns of resistance of the prevalent serotypes other than *S. wien*; *S. heidelberg* showed a high multiple resistance (50%).

A preliminary study about the presence of R plasmids was performed on 46 strains of *S. typhimurium*, 12 of which were resistant to a single antimicrobial agent, with 34 showing a multiple resistance. R plasmids have been found in 21 strains (46%); they have been carried in 33% of mono-resistant strains, in 50% of strains which were resistant to two or more antimicrobials and in 65% of strains which showed a resistance to three or more antimicrobials. Table 8 shows the results of transfer of such R-plasmids.

DISCUSSION

From this study antibiotic resistance seems to occur commonly among salmonella isolates from hospitals. The overall prevalence of antimicrobial resistance was deeply affected by the number of resistant strains of *S. wien*, whose typical multiple resistance has been described in Italy and in other Mediterranean countries

Table 7. Resistance patterns of prevalent salmonella serotypes, other than *S. wien*

Resistance pattern*	Number with pattern in each serotype							Total
	<i>S. typhimurium</i>	<i>S. enteritidis</i>	<i>S. panama</i>	<i>S. livingstone</i>	<i>S. infantis</i>	<i>S. heidelberg</i>	Others	
Sensitive	45	34	16	14	12	2	107	230
Su	13	6	14	7	3	2	41	86
T	13	3	1	—	—	1	4	22
SuT	10	—	—	—	—	—	3	13
SSu	6	1	1	—	—	1	3	12
ST	8	—	—	—	—	—	1	9
SSuT	5	—	1	—	—	—	2	8
S	4	—	—	—	—	—	3	7
SuTm	—	—	—	1	1	—	4	6
ACKSSuT	2	—	—	—	1	2	—	5
ACSSu	1	2	—	—	—	—	1	4
AS	2	—	—	—	—	—	—	2
AKS	2	—	—	—	—	—	—	2
ASSu	1	—	—	—	—	—	—	2
KST	—	—	1	—	—	—	1	2
CKSSuT	2	—	—	—	—	—	—	2
CSSuTTm	2	—	—	—	—	—	—	2
ACCeKSSuT	1	1	—	—	—	—	—	2
Other 21 patterns	6	1	3	—	1	2	8	21
Total	123	48	37	22	18	10	179	437

* Abbreviations as in Materials and Methods.

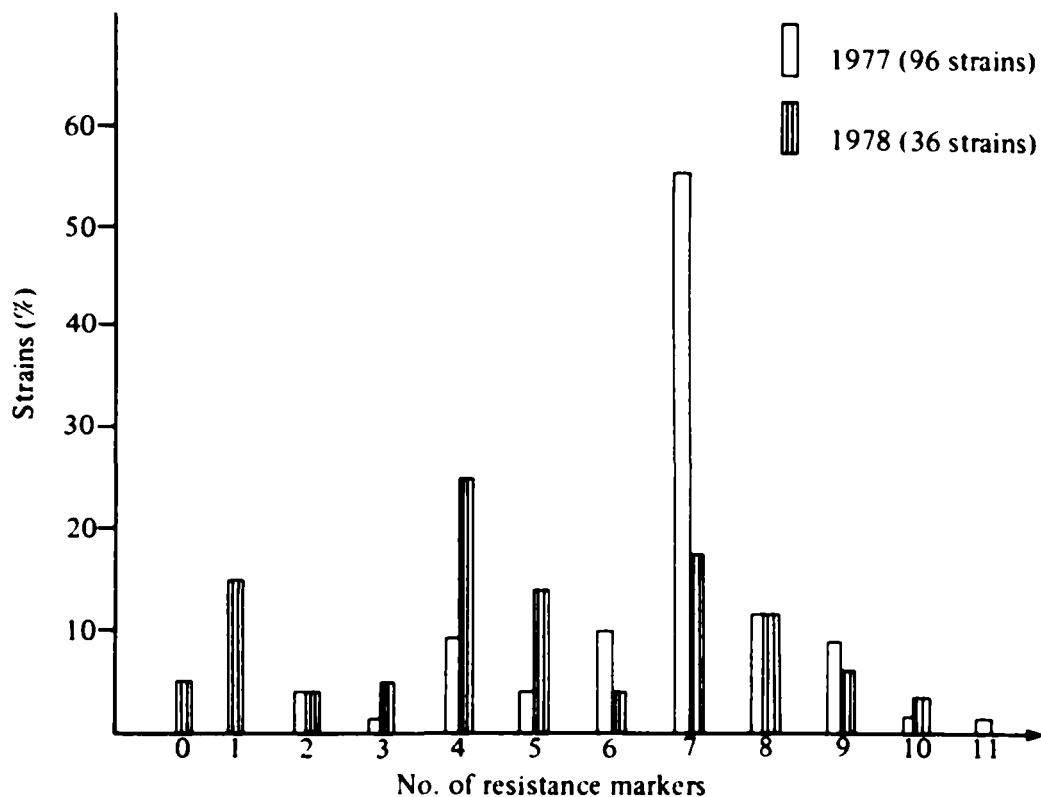


Fig. 1. Antimicrobial resistance variations in *S. wien*.

(Marranzano *et al.* 1976; Mered *et al.* 1970; Le Minor, 1972; Brisou, Bardon & Menard, 1972; Paradelis & Stathopoulos, 1978). A high prevalence rate of resistance is evident also for other serotypes, with the highest values for *S. typhimurium* and *S. panama*.

According to studies performed on salmonella strains in North Italy (Luppi *et al.* 1973; Pitzus *et al.* 1975), Netherlands (Voogd *et al.* 1973, 1977), Canada (Grant & Di Mambro, 1976; Duck *et al.* 1978), USA (Winshell *et al.* 1970; Bissett, Abbott & Wood, 1974; Neu *et al.* 1975) a high percentage of multiple resistance among *S. typhimurium* strains has been found.

Similarly a high number of multiple-resistant strains of *S. heidelberg* has been observed, agreeing with Duck *et al.* (1978) and Bissett *et al.* (1974); however, the number of strains has been too low to be significant. All strains of *S. typhi* are still considerably sensitive to all tested antimicrobials, which may be of great help in the treatment of the still highly prevalent cases of typhoid fever.

The most frequent resistance was to sulphathiazole, tetracycline and streptomycin. Most of the resistance to ampicillin, chloramphenicol, kanamycin and cephalothin was due to *S. wien* strains, whereas the overall percentage of resistance of the other serotypes was quite low: 2.3% to chloramphenicol, 4.8% to kanamycin, 2.3% to cephalothin, 7.1% to ampicillin.

Change in the pattern of resistance of *S. wien* may be considered very interesting: the ACCeKSSuT pattern was the most frequent in 1977 (47%) as previously described by Marranzano *et al.* (1976), Abbate *et al.* (1977), McConnell *et al.* (1979).

In 1978 an increase in the susceptibility of *S. wien* to some antimicrobial agents (such as sulphathiazole, chloramphenicol, streptomycin, tetracycline) which were

Table 8. Drug resistance transfer from *S. typhimurium* strains isolated during the period 1977–8, to *E. coli* K12

Resistance pattern*	No. of strains	No. of R. plasmids carrier strains	Transferred markers
T	8	2	T
S	3	1	S
K	1	1	K
SuT	6	—	—
ST	5	2	ST
SSu	3	1	SSu
KTm	1	1	KTm
AS	2	2	AS
SSuT	5	3	SSuT
AKS	2	2	AKS
ASSu	1	—	—
ASSuT	1	1	ASSu
CSSuT	1	1	CSSuT
AKSSuT	1	1	AKSSuT
CSSuTm	2	2	CSSuTm
ACKSSuT	2	1	ACKSSuT
ACCeClSSuT	1	—	—
ACCeKSSuT	1	—	—
Total	46	21	

* Abbreviations as in Materials and Methods.

previously almost ineffective against this serotype has been observed, together with an increase of resistance to gentamicin and tobramycin, according to Altucci *et al.* (1977).

The large number of resistant isolates and the high prevalence rate of R-plasmid carriers among the resistant strains of *S. typhimurium* confirm the danger of an increasing 'selective pressure', particularly in a hospital environment, in which the great misuse of antibiotics plays an important role.

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