Antimicrobial susceptibility of *Salmonella*, 2015

Hospital and community laboratories are requested to refer all *Salmonella* isolated from human salmonellosis cases to ESR for serotyping and the laboratory-based surveillance of this disease. *Salmonella* from other sources, including food, animal and environmental sources, are also referred to ESR for typing. The antimicrobial susceptibility of a sample (approximately 20%) of non-typhoidal *Salmonella* isolates and all typhoidal isolates is routinely tested at ESR. In addition, the susceptibility of all isolates belonging to internationally recognised multidrug-resistant *Salmonella* clones is tested. These clones include *S.* Typhimurium phage types DT12, DT104, DT120, DT193 and U302, and *S. enterica* serovar 4,[5],12:i:-.

Antimicrobial susceptibility is determined by the Clinical and Laboratory Standards Institute's (CLSI's) disc diffusion method.[1] All cephalothin-resistant isolates are further tested for the production of extended-spectrum β-lactamase (ESBL) and plasmid-mediated AmpC β-lactamase (PMACBL). Multidrug resistance is defined as resistance to ≥3 antibiotic classes. Overseas travel history for human salmonellosis cases was obtained from information reported in the EpiSurv notifiable disease database supplemented with any additional travel information received when the isolate from the case was referred to ESR.

Non-typhoidal Salmonella

In 2015, the antimicrobial susceptibility of a representative sample of 355 non-typhoidal *Salmonella* was tested. The sample comprised 235 isolates from human sources and 120 food/animal/environmental isolates.

Resistance to each of the 11 antimicrobials tested and multidrug resistance is shown in Table 1. Antimicrobial resistance among *Salmonella* remains relatively low, with 89.3% (86.0% of human isolates and 95.8% of food/animal/environmental isolates) fully susceptible to all 11 antimicrobials.

Four (1.7%) of the *Salmonella* from human sources tested in 2015 produced a β-lactamase that would confer resistance to 3rd-generation cephalosporins such as ceftriaxone. Two of these isolates produced an ESBL and the other two a CMY-2-like PMACBL. One of the cases with an ESBL-producing isolate (*S.* Rissen) and one with a PMACBL-producing isolate (*S.* Heidelberg) had recently travelled overseas to Thailand and the Philippines, respectively.

No isolates in the representative sample of 355 non-typhoidal *Salmonella* were ciprofloxacin resistant. However, 30 (8.5%) isolates had intermediate ciprofloxacin resistance: 25 (10.6%) from human sources and 5 (4.2%) from other sources (ie, food, animal and environmental sources). Patients infected with *Salmonella* strains that test as ciprofloxacin intermediate may fail fluoroquinolone treatment or have a delayed response to such treatment.

Salmonella from human sources were significantly ($P < 0.05$) more resistant to ampicillin, streptomycin and tetracycline, and more multidrug resistant, than *Salmonella* from other sources (Table 1). Resistance to ampicillin and streptomycin, and multidrug resistance, was still significantly more prevalent among *Salmonella* from human sources when the comparison was confined to only human salmonellosis cases who had no reported recent overseas travel.

Table 1. Antimicrobial resistance among non-typhoidal *Salmonella*, 2015

Antimicrobial	Percent resistant			P value for significance of any difference in resistance between human and other isolates[1]
	All isolates n = 355	Human isolates n = 235	Food/animal/ environmental isolates n = 120	
Ampicillin	6.8	10.2	0.0	<0.001
Amoxicillin-clavulanate	1.7	2.6	0.0	0.100
Cephalothin[2]	1.4	2.1	0.0	0.172
Chloramphenicol	1.7	2.6	0.0	0.101
Ciprofloxacin	0.0	0.0	0.0	-
Co-trimoxazole	2.0	3.0	0.0	0.100
Gentamicin	0.6	0.9	0.0	0.551
Streptomycin	4.2	6.0	0.8	0.023
Sulphonamides	5.4	6.8	2.5	0.088
Tetracycline	5.6	7.7	1.7	0.021
Trimethoprim	2.0	3.0	0.0	0.100
Multiresistant to ≥3 antimicrobials[3]	5.1	7.7	0.0	0.002

1 Chi-square test or Fisher's Exact test as appropriate.

2 There were five cephalothin-resistant isolates, which were all from human salmonellosis cases. Two of these isolates produced extended-spectrum β-lactamase (ESBL) and another two produced CMY-2-like plasmid-mediated AmpC β-lactamase.

3 For estimates of multidrug resistance, co-trimoxazole and trimethoprim resistance was counted as one resistance.

Table 2 shows a comparison of resistance among isolates from salmonellosis cases reported to have recently travelled overseas with isolates from cases for whom no recent overseas travel was reported. While *Salmonella* isolates from people who had travelled were consistently more resistant, the difference was only significant ($P < 0.05$) for ampicillin and tetracycline.

Table 2. Antimicrobial resistance among non-typhoidal *Salmonella* from cases who had travelled overseas compared with non-travellers, 2015

Antimicrobial	Percent resistant		P value for significance of any difference in resistance between travellers and non-travellers[1]
	Cases who had travelled overseas n = 70	Cases who had not travelled overseas n = 165	
Ampicillin	17.1	7.3	0.022
Amoxicillin-clavulanate	2.9	2.4	1.000
Cephalothin	2.9	1.8	0.636
Chloramphenicol	4.3	1.8	0.367
Ciprofloxacin	0.0	0.0	-
Co-trimoxazole	4.3	2.4	0.428
Gentamicin	1.4	0.6	0.508
Streptomycin	7.1	5.5	0.764
Sulphonamides	10.0	5.5	0.257
Tetracycline	12.9	5.5	0.051
Trimethoprim	4.3	2.4	0.428
Multiresistant to ≥3 antimicrobials[2]	11.4	6.1	0.182

1 Chi-square test or Fisher's Exact test as appropriate.
2 For estimates of multidrug resistance, co-trimoxazole and trimethoprim resistance was counted as one resistance.

In 2015, several isolates belonging to internationally recognised multidrug-resistant *Salmonella* clones were identified and tested. These included:

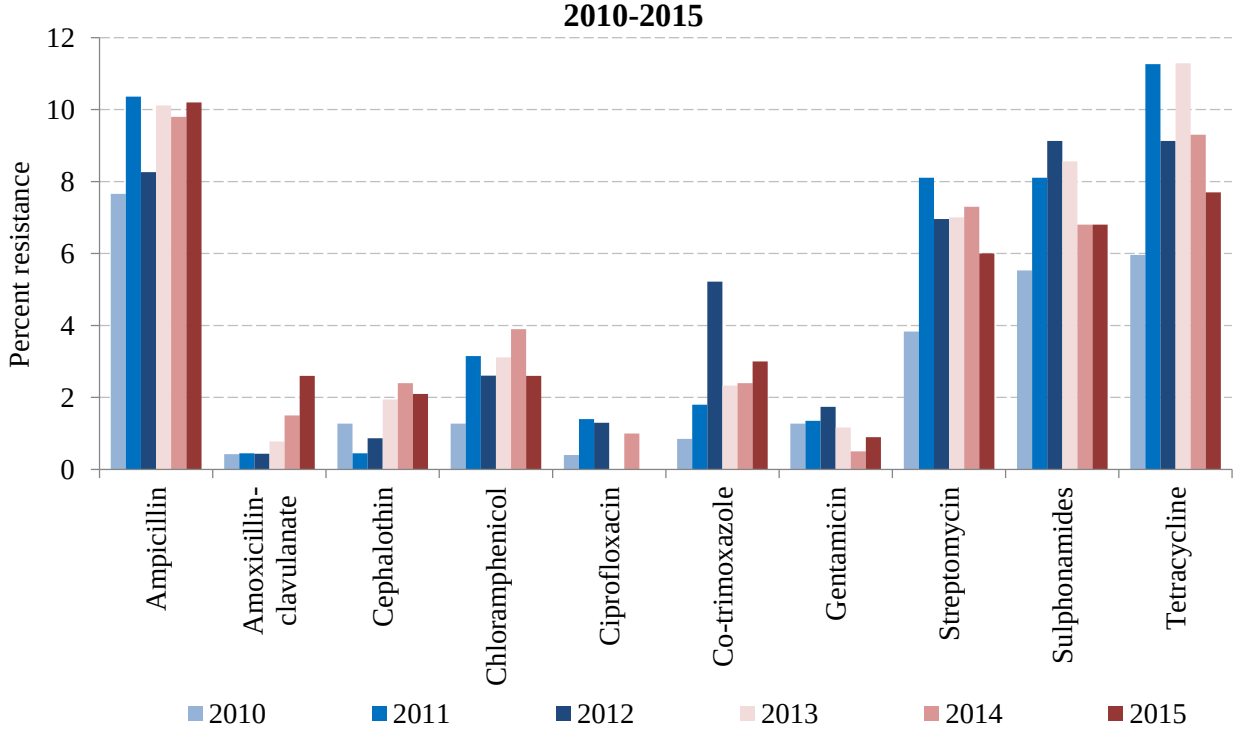
- 18 isolates of *S.* Typhimurium phage type DT193, with equal numbers (ie, nine) from human sources and non-human sources. Seven (five from human sources and two from non-human sources) of the 18 isolates were multidrug resistant. The multiresistant patterns were variable, but notably one of the resistance patterns of an isolate from a human source included ciprofloxacin resistance.
- 1 isolate of *S.* Typhimurium phage type DT104. This isolate was from a human source. The isolate had the multiresistant pattern typical for this phage type, that is, resistant to ampicillin, chloramphenicol, streptomycin, sulphonamides and tetracycline.

No isolates of the other internationally recognised multidrug-resistant *S.* Typhimurium clones, that is, DT12, DT120 or U302, were identified in 2015.

S. enterica serovar 4,[5],12:i:- is a monophasic variant of *S.* Typhimurium, and isolates are typically multidrug resistant to ampicillin, streptomycin, sulphonamides and tetracycline. This serovar is now among the 10 most common *Salmonella* serovars isolated from humans in many countries in Europe, and it was the tenth most common in New Zealand in 2015. Thirty-three isolates of *S. enterica* serovar 4,[5],12:i:- were identified in New Zealand in 2015, and all but one were from human salmonellosis cases. 27 (81.8%) of the 33 isolates were multidrug resistant, with 18 of the 27 multidrug-resistant isolates having the resistance pattern typical of this serovar (ie, resistant to at least ampicillin, streptomycin, sulphonamides and tetracycline). The resistance pattern of one of the multidrug-resistant isolates included ciprofloxacin resistance. Travel history was reported for 25 of the 27 multidrug-resistant cases, 23 of whom had recently travelled overseas with the country or region reported for 22 cases: Thailand (6 cases), Indonesia (6), China (3), Cambodia (2), Vietnam (1), Hong Kong (1), multiple Southeast Asian countries (1), Turkey (1) and Australia (1).

Trends in resistance among *Salmonella* from human cases since 2010 are shown in Figure 1. There has been a significant ($P < 0.05$) increase in amoxicillin-clavulanate resistance over the last 6 years.

Figure 1. Resistance among non-typhoidal *Salmonella* from human cases, 2010-2015



Trimethoprim resistance not shown as the rates of co-trimoxazole and trimethoprim resistance are almost invariably the same. The ciprofloxacin resistance rates for all years shown are based on the CLSI interpretive standards revised in 2013.

Typhoidal Salmonella

In 2015, 46 *S.* Typhi and 13 *S.* Paratyphi A isolates were referred to ESR. Resistance among these typhoidal *Salmonella* to each of the 12 antimicrobials tested is shown in Table 3.

None of the 46 *S.* Typhi isolates were multidrug resistant. Two (4.3%) isolates were ciprofloxacin resistant and another 21 (45.7%) isolates had intermediate ciprofloxacin resistance. Travel history was recorded 17 of the 23 people from whom ciprofloxacin non-susceptible *S.* Typhi were isolated, and 15 of these 17 people had recently travelled to the Indian subcontinent. Due to the emergence of ciprofloxacin non-susceptibility among *S.* Typhi in the Indian subcontinent and Southeast Asia, azithromycin is now the recommended treatment for typhoid fever. One (2.2%) of the 46 *S.* Typhi isolates tested in 2015 was azithromycin resistant. This isolate was one of the two ciprofloxacin-resistant *S.* Typhi. No travel history was recorded for the person from whom this azithromycin- and ciprofloxacin-resistant *S.* Typhi was isolated.

None of the 13 *S.* Paratyphi A isolates were multidrug resistant. While none of the *S.* Paratyphi A isolates were ciprofloxacin resistant, 11 (84.6%) isolates had intermediate ciprofloxacin resistance. Travel history was recorded for 9 of the 11 people from whom ciprofloxacin non-susceptible *S.* Paratyphi A were isolated, and 8 of these 9 people had recently travelled to the Indian subcontinent.

Table 3. Antimicrobial resistance among *Salmonella* Typhi and *S*. Paratyphi, 2015[1]

Antimicrobial	Percent (number) resistant	
	***S*. Typhi n = 46**	***S*. Paratyphi A n = 13**
Ampicillin	0.0 (0)	0.0 (0)
Amoxicillin-clavulanate	0.0 (0)	0.0 (0)
Azithromycin	2.2 (1)	-[2]
Cephalothin	0.0 (0)	0.0 (0)
Chloramphenicol	0.0 (0)	0.0 (0)
Ciprofloxacin	4.3 (2)	0.0 (0)
Co-trimoxazole	0.0 (0)	0.0 (0)
Gentamicin	0.0 (0)	0.0 (0)
Streptomycin	15.2 (7)	0.0 (0)
Sulphonamides	0.0 (0)	0.0 (0)
Tetracycline	0.0 (0)	0.0 (0)
Trimethoprim	0.0 (0)	0.0 (0)
Multiresistant to ≥3 antimicrobials[3]	0.0 (0)	0.0 (0)

1 There were no *S*. Paratyphi B isolates referred to ESR in 2015 and *S*. Paratyphi B var Java isolates are not included with the *S*. Paratyphi isolates, as they are no longer considered to belong to the typhoidal *Salmonella*.

2 There are no CLSI azithromycin interpretive standards for *S.* Paratyphi.

3 For estimates of multidrug resistance, co-trimoxazole and trimethoprim resistance was counted as one resistance.

[1] Clinical and Laboratory Standards Institute. Performance standards for antimicrobial susceptibility testing; twenty-fifth informational supplement. Wayne, PA, USA: CLSI; 2015. CLSI document M100-S25.