

Increase in Multidrug-resistant *Salmonella* Serotype I 4,[5],12:i:- Infections Linked to Pork—United States, 2009–2018

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Background

Salmonella enterica I 4,[5],12:i:-

- Nontyphoidal *Salmonella* cause ~1.2 million illnesses and 23,000 hospitalizations per year in the United States.
- I 4,[5],12:i:- is a monophasic variant of *Salmonella* Typhimurium and is the 5th most common serotype causing clinical infections.

Multidrug-resistant I 4,[5],12:i:-

- A multidrug-resistant (MDR) strain of I 4,[5],12:i:- has been increasingly reported globally that has resistance to ampicillin, streptomycin, sulfamethoxazole, and tetracycline (ASSuT), and intolerance to heavy metals used in animal feed. This strain has been identified during pig production and in outbreaks from contaminated pork.
- We evaluated clinical infections with MDR I 4,[5],12:i:- in the United States during 2009–2018.

Methods

We analyzed data from several U.S. national surveillance systems for *Salmonella* infections:

- We analyzed whole-genome sequence data in PulseNet, the molecular surveillance network for foodborne illness, from 2015–2018 to distinguish between strains of I 4,[5],12:i:- using core-genome multilocus sequence typing (cgMLST). We assigned predicted antibiotic resistance from genetic resistance determinants, and used the NCBI pathogen detection portal to assess relatedness to reported strains.
- We reviewed historical PulseNet data from 2009–2018 to assess trends in isolates with pulse-field gel electrophoresis (PFGE) patterns found in the cgMLST clade.
- We reviewed data from CDC’s National Antimicrobial Resistance Monitoring System (NARMS) from 2009–2018 to describe trends in phenotypic resistance.
- We compared reports of I 4,[5],12:i:- outbreaks during 2009–2018 in the National Outbreak Reporting System (NORS) according to whether the outbreak PFGE patterns were found in the cgMLST clade.

Results

Figure 1: Phylogenetic clustering and predicted resistance of sequenced clinical isolates in PulseNet identified as *Salmonella* I 4,[5],12:i:- or Typhimurium— United States, 2015–2018

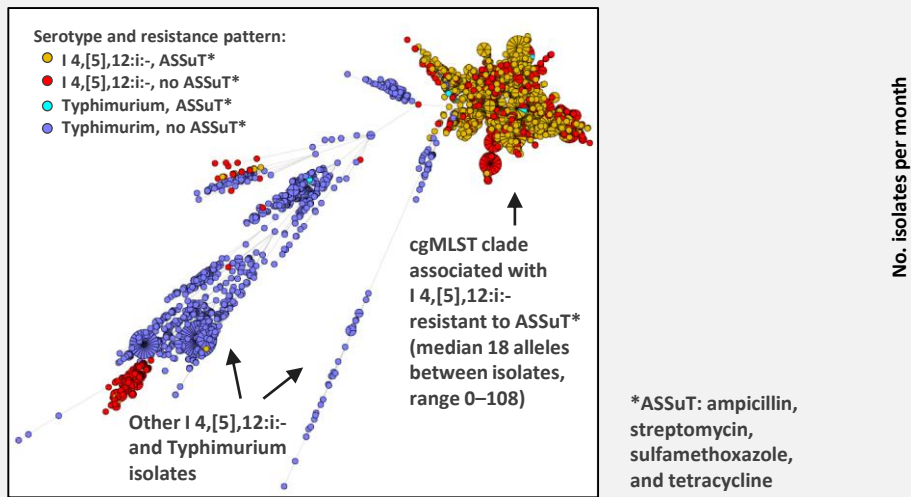


Table 1: Predicted resistance of sequenced isolates of *Salmonella* I 4,[5],12:i:- by membership on the cgMLST clade — United States, 2015–2018

Predicted resistance	<i>Salmonella</i> I 4,[5],12:i:-	<i>Salmonella</i> I 4,[5],12:i:- in cgMLST clade	<i>Salmonella</i> I 4,[5],12:i:- not in cgMLST clade	Odds ratio (95% CI) for cgMLST clade
ASSuT*	1657/3051 (54.3%)	1624/2100 (77.3%)	33/951 (3.5%)	94.91 (66.08-136.31)
Ciprofloxacin	324/3051 (10.6%)	275/2100 (13.1%)	49/951 (5.2%)	2.77 (2.03-3.8)
Ceftriaxone	135/3051 (4.4%)	113/2100 (5.4%)	22/951 (2.3%)	2.4 (1.51-3.82)
Azithromycin	14/3051 (0.5%)	11/2100 (0.5%)	3/951 (0.3%)	1.66 (0.46-5.98)

Table 2: Characteristics of outbreaks of *Salmonella* I 4,[5],12:i:- infections reported to the National Outbreak Reporting System — United States, 2009–2018

	Outbreaks from <i>Salmonella</i> I 4,[5],12:i:- (n=121)	Outbreaks with PFGE patterns found in the cgMLST clade (n=71‡)	Outbreaks with PFGE patterns not found in the cgMLST clade (n=43‡)
Mode of transmission			
Foodborne	73/121 (60%)	39/71 (55%)	31/43 (72%)
Animal contact	18/121 (15%)	12/71 (17%)	5/43 (12%)
Person to person	7/121 (6%)	6/71 (8%)	1/43 (2%)
Other or unknown	23/121 (19%)	14/71 (20%)	6/43 (14%)
Food category (if single category)			
Pork	12/21 (57%)	10/15 (67%)	1/5 (20%)
Chicken	3/21 (14%)	2/15 (13%)	1/5 (20%)
Turkey	2/21 (10%)	2/15 (13%)	0/5 (0%)
Dairy	1/21 (5%)	1/15 (7%)	0/5 (0%)
Other food source	3/21 (1%)	0/15 (0%)	3/5 (60%)
Animal contact (if single animal)			
Pig	5/13 (38%)	5/9 (56%)	0/4 (0%)
Poultry	3/13 (23%)	2/9 (22%)	1/4 (25%)
Cattle	1/13 (8%)	1/9 (11%)	0/4 (0%)
Other animal	4/13 (31%)	1/9 (11%)	3/4 (75%)

‡Excludes 7 *Salmonella* I 4,[5],12:i:- outbreaks with unknown PFGE pattern

Figure 2: Clinical isolates submitted to PulseNet identified as *Salmonella* I 4,[5],12:i:- by PFGE pattern — United States, 2009–2018

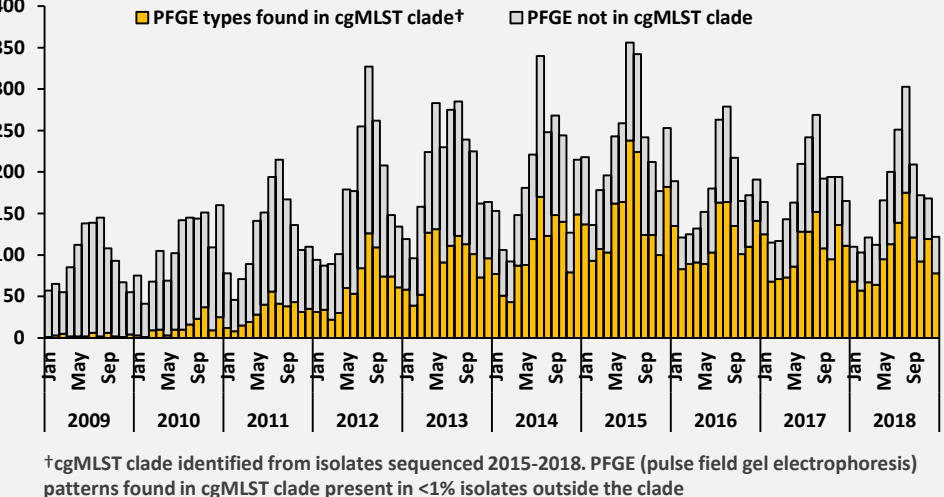
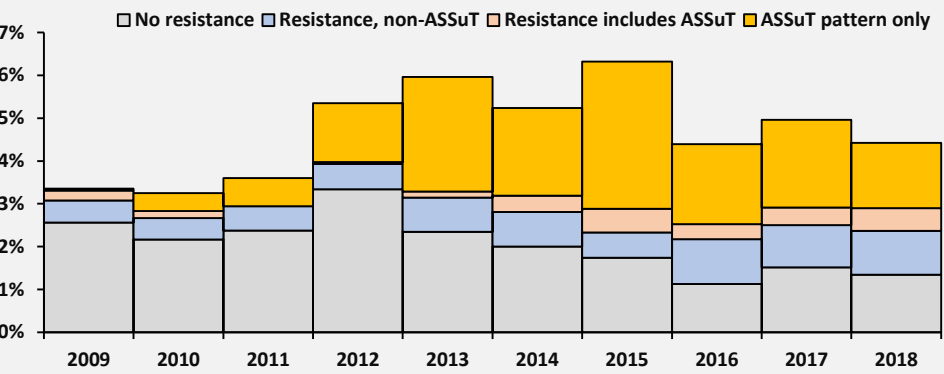


Figure 3: Proportion of nontyphoidal *Salmonella* isolates submitted to NARMS surveillance that were I 4,[5],12:i:- by antibiotic resistance pattern — United States, 2009–2018



- Among 3,056 sequenced I 4,[5],12:i:- isolates in PulseNet, 2,105 (69%) were in a cgMLST clade associated with ASSuT resistance (Figure 1). Isolates in this clade contained the same resistance genes and genomic island (conferring heavy metal intolerance) characterized by other studies. Isolates with PFGE patterns found in the clade increased since 2010 (Figure 2).
- From 2009–2013 to 2014–2018, I 4,[5],12:i:- increased as a proportion of nontyphoidal *Salmonella* isolates in NARMS from 4.3% to 5.0% ($P<0.001$), while I 4,[5],12:i:- resistant to ASSuT increased from 1.1% to 2.6% ($P<0.001$; Figure 3).
- Isolates in the clade were more likely than others to have predicted resistance to ciprofloxacin or ceftriaxone (Table 1).
- Among I 4,[5],12:i:- outbreaks with a single food source, those with PFGE patterns found in the cgMLST clade were more often linked to pork (10/15 [67%] vs. 1/5 [20%], $P=0.07$; Table 2).

Conclusions

Clinical infections from *Salmonella* I 4,[5],12:i:- increased because of an increase in a multidrug resistant clade

- An increase in *Salmonella* infections with I 4,[5],12:i:- was caused by an increase in isolates resistant to ASSuT that were closely related to strains reported elsewhere.
- In the United States, the expansion of a clade associated with ASSuT resistance likely began in 2010.
- By 2015–2018, nearly 70% of I 4,[5],12:i:- infections were from isolates linked to the multidrug resistant clade.

Salmonella I 4,[5],12:i:- from the multidrug resistant clade might not respond to recommended antibiotics

- During 2015–2018, 13% of isolates in the clade had predicted resistance to ciprofloxacin, and 5% had predicted resistance to ceftriaxone.
- Resistance to ciprofloxacin and ceftriaxone was more likely among I 4,[5],12:i:- isolates within the clade.
- This could limit treatment options for patients with invasive *Salmonella* infections.

Human illness from multidrug resistant *Salmonella* I 4,[5],12:i:- might be prevented by limiting infections in swine

- Outbreaks of I 4,[5],12:i:- from the MDR clade were more likely to be linked to pork consumption, consistent with evidence from other studies.
- Human illness from organisms in this clade might be prevented by implementing measures to decrease *Salmonella* contamination of pork, and by limiting unnecessary use of antibiotics or heavy metals that could select for this clade among swine herds.

Contact Info

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