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Editorial

Why are we still detecting food-related *Salmonella* outbreaks in Spain?

¿Por qué estamos detectando aún brotes de *Salmonella* relacionados con la alimentación en España?

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Salmonella enterica is one of the leading causes of foodborne infections, and until 2005 it was the most common food-borne pathogen in the European Union (EU). However, the implementation of control measures has reduced the burden of salmonellosis resulting in a reduction in the number of human *Salmonella* cases by almost 50% over five years (2004–2009) with a concomitant, significant fall in the prevalence of *Salmonella* in poultry.

Despite these efforts, 94 million cases of gastroenteritis occur worldwide every year with 155,000 deaths being attributed to the genus *Salmonella* of which Enteritidis followed by Typhimurium are the most prevalent serovars.[1–3] In terms of economic burden and according to the European Food Safety Authority (EFSA) it has been estimated that the overall cost of human salmonellosis for the EU may be of up to 3 billion euros per year.

However, in the last decade a new serovar, the monophasic *S.* Typhimurium 1,4,[5],12:i:- lacking the second-phase H antigen,:-, encoded by *fljB*, has emerged and has become the third most common *Salmonella* serovar in Europe.[3–5] Moreover, outside Europe this emergent serovar has already caused a substantial number of outbreaks in several countries including Brazil[6] and the United States.[7]

Regarding *Salmonella* causing infection in humans, according to the last report from the EFSA, a high proportion of the isolates recovered in the EU are resistant to ampicillin (36.1%), sulfonamides (35.7%) and tetracyclines (34.5%), whereas low levels of resistance to third-generation cephalosporins and fluoroquinolones have been reported. Almost one-third of these isolates showed multidrug resistance (MDR) (31.8%), and in Spain this proportion was 72.4%, being the country with the highest proportion after Luxembourg (85.2%) and Estonia (78.3%). Interestingly, isolates belonging to the monophasic *S.* Typhimurium 1,4,[5],12:i:- were highly multiresistant (83.8%) followed by *S.* Kentucky (67.3%).[8]

Most of the antibiotics used to treat salmonellosis in the clinical setting coincide with those used to prevent and treat food-producing animals. Consequently, *Salmonella* isolated from food and animals show a similar antimicrobial resistance profile (resistance to sulfonamides and tetracyclines, and to a lesser extent ampicillin). Isolates recovered from pigs and turkeys show higher levels of resistance than those from broilers, hens and cattle.[9] Concerning fluoroquinolones, which are widely recommended to treat invasive salmonellosis in adult humans, the highest levels of resistance in the animal setting have been reported in *Salmonella* spp. isolates recovered from broilers, laying hens and pigs in some EU countries, including Spain. However, in general terms, from 2007 to 2013 a decrease was reported in the trends of resistance to ciprofloxacin in Europe. Resistance to nalidixic acid is generally higher in *S.* Enteritidis isolates from humans than in *S.* Typhimurium.[9] An exception to this scenario is the increase of resistance to ciprofloxacin observed in some countries and likely associated with the prevalence of a high-risk clone of *S.* Kentucky ST198-X1 resistant to ciprofloxacin. In addition, the overall slight increase of resistance to ciprofloxacin in *Salmonella* isolates from humans observed in 2014 (8.8%) compared to 2013 (3.8%) is most likely due to a combination of the lowering of the clinical breakpoints for ciprofloxacin by the EUCAST in 2014, making them now directly comparable with the epidemiological cut-off values (ECOFFs), and the implementation by a few countries of a better marker (pefloxacin) than ciprofloxacin for screening of low-level fluoroquinolone resistance in *Salmonella* by disk diffusion.[9]

In *Salmonella enterica* it has previously been reported that acquisition of ciprofloxacin resistance *in vitro* is related to a decrease in virulence and the ability to invade eukaryotic cells[10,11]; thus, this, together with the *Salmonella* control programs implemented may have also contributed to the decrease in the incidence of ciprofloxacin resistance despite the increase in the prevalence of nalidixic acid-resistant isolates.

Interestingly, in recent years there has been a decrease in the prevalence of isolates of *S.* Typhimurium belonging to the MDR phage type PT104 and the emergence of the monophasic serovar 4,[5],12:i:- resistant to multiple antibiotics (mainly ampicillin, streptomycin, sulphonamides and tetracyclines) in several European countries,[9,12,13] including Spain. As shown in two studies

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published in the current issue of this journal[14,15] and according to the last EFSA report,[9] most monophasic *S.* Typhimurium isolated in Spain were recovered from fattening pigs. In the first study, Hernández-Arricibita and colleagues[14] described an outbreak affecting six people associated with the consumption of chorizo contaminated with monophasic variants 4,[5],12:i:-. In the second study by Arnedo-Pena and colleagues,[15] the source of the outbreak was dried pork sausage and was caused by several isolates of *S.* Typhimurium, including serovar 4,[5],12:i:-and *S.* Derby.

Although the monophasic variant 1,4,[5],12:i:- has gained increasing importance in many European countries and has also recently been reported in China,[16] it seems that this is also the case for the monophasic *S.* Typhimurium serovar 4,[5],12:i:-, that has spread in countries such as Spain, with swine being the most likely reservoir.[17] In fact, this serovar is currently one of the most common serovars responsible for salmonellosis in humans not only in Europe but also the United States after having caused several recent outbreaks there.[18] In a study performed in Spain,[19] *Salmonella* spp. were isolated in 31% of pigs and 94% of herds, being monophasic variant 4,[5],12:i:- the most prevalent. The high prevalence of *Salmonella* in herds was associated with a lack of rodent control, farms with only finishing pigs, managed by more than one full-time worker and relatively long fattening times. Other potential risk factors related to herds with *Salmonella* were pelleted feed, farms where birds were visible inside the fattening units and farms that shared workers with other pig farms.[20] Therefore, feeding, hygiene and management measures can help to control these factors. Most of the national monitoring programs for *Salmonella* in pigs are focused on pig meat and products and are based on sampling at the slaughterhouse by swabbing a part of the carcass and/or at the processing or cutting plants where meat samples are usually collected.[3] In a Spanish study carried out by Arguello and colleagues[21] it was found that not only the farm but also the transport and especially the lairage contributed to *Salmonella* contamination in pigs, and that the slaughtering procedure is an important source of carcass contamination.

Control measures are needed in order to prevent the pandemic spread of this emerging serovar and avoid the situation that occurred in the 1990s with *S.* Typhimurium DT104. In this particular case, appropriate interventions mainly focused on pig husbandry should be implemented in the EU. In this sense, it must be emphasized that *Salmonella* control programs in poultry and laying hens have been established in most European countries leading to a decrease in the prevalence of *Salmonella* in poultry. On the other hand, the number of contaminated pork products has been on the rise due to the lack of compulsory control programs in pig production. Therefore, control programs for *Salmonella* in pigs should be mandatory for farms, slaughterhouses and cutting plants, with especial attention to transport and lairage.

In addition to foodborne transmission of resistant pathogens, population and animal movements, as well as international food trade and farming procedures also contribute to pathogen dissemination. Therefore, it is important to concentrate efforts on the implementation of new measures and reinforcement of current programs at different levels.

In the food industry antibiotic consumption should be restricted in food-producing animals particularly for non-therapeutic use, and alternative treatment strategies should be applied. Additionally, antibiotics should be carefully selected to avoid cross-resistance in the clinical setting. Improvement of hygiene measures in both animal handling and along the food chain production should also be reinforced through control measures and training programs addressed to professionals in this field such as farm workers, veterinarians and food handlers. At a clinical level, antimicrobial stewardship programs should be established in hospitals in order to provide the most suitable treatment to patients taking into account the local context.

Tackling the spread of resistant clones such as the monophasic *S.* Typhimurium serovar4,[5],12:i:- is a complicated task. It is evident that the current strategies are not efficient enough, making a multifaceted approach at both local and global levels necessary to fight against the increasing menace of antimicrobial resistance.

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References

1. Majowicz SE, Musto J, Scallan E, Angulo FJ, Kirk M, O'Brien SJ, et al. The global burden of nontyphoidal *Salmonella* gastroenteritis. Clin Infect Dis. 2010;50:882–9.
2. Incidence and trends of infection with pathogens transmitted commonly through food. Morb Mortal Wkly Rep. 2013;62:283–7.
3. European Food Safety Authority. The European Union summary report on trends and sources of zoonoses, zoonotic agents and food-borne outbreaks in 2013. EFSA J. 2015;13:3391.
4. Mossong J, Marques P, Ragimbeau C, Huberty-Krau P, Losch S, Meyer G, et al. Outbreaks of monophasic *Salmonella enterica* serovar 4,[5],12:i:- in Luxembourg, 2006. Euro Surveill. 2007;12:156–8.
5. Gallati C, Stephan R, Hachler H, Malorny B, Schroeter A, Nuesch-Inderbinen M. Characterization of *Salmonella enterica* subsp. *enterica* serovar 4,[5],12:i:- clones isolated from human and other sources in Switzerland between 2007 and 2011. Foodborne Pathog Dis. 2013;10:549–54.
6. Tavechio AT, Ghilardi AC, Fernandes SA. "Multiplex PCR" identification of the atypical and monophasic *Salmonella enterica* subsp. enterica serotype 1,4,[5],12:i:- in Sao Paulo State, Brazil: frequency and antibiotic resistance patterns. Rev Inst Med Trop Sao Paulo. 2004;46:115–7.
7. Agasan A, Kornblum J, Williams G, Fleckenstein P, Wong M, Ramon A, et al. Profile of *Salmonella enterica* subsp. strains causing food-borne infections in New York City profile of *Salmonella enterica* subsp. *enterica* (subspecies I) serotype 4,5,12:i:- strains causing food-borne infections in New York City. J Clin Microbiol. 2002;40:1924–9.
8. EU Summary Report on antimicrobial resistance in zoonotic and indicator bacteria from humans, animals and food in 2013. EFSA. J. 2015;13: 4036.
9. European Food Safety Authority. EU Summary Report on antimicrobial resistance in zoonotic and indicator bacteria from humans, animals and food in 2014. EFSA J. 2016;14:4380.
10. Fàbrega A, Soto SM, Ballesté-Delpierre C, Fernández-Orth D, Jiménez de Anta MT, Vila J. Impact of quinolone-resistance acquisition on biofilm production and fitness in *Salmonella enterica*. J Antimicrob Chemother. 2014;69: 1815–24.
11. Fàbrega A, du Merle L, Le Bouguénec C, Jiménez de Anta MT, Vila J, Fabrega A, et al. Repression of invasion genes and decreased invasion in a high-level fluoroquinolone-resistant *Salmonella* Typhimurium mutant. PLoS ONE. 2009;4:e8029.
12. Meakins S, Fisher IST, Berghold C, Gerner-Smidt P, Tschape H, Cormican M, et al. Antimicrobial drug resistance in human nontyphoidal *Salmonella* isolates in Europe 2000–2004: a report from the Enter-net International Surveillance Network. Microb Drug Resist. 2008;14:31–5.
13. Vico JP, Rol I, Garrido V, San Román B, Grilló MJ, Mainar-Jaime RC. Salmonellosis in finishing pigs in Spain: prevalence, antimicrobial agent susceptibilities, and risk factor analysis. J Food Prot. 2011;74:1070–8.
14. Arnedo-Pena A, Sabater-Vidal S, Herrera-León S, Bellido-Blasco JB, Silvestre-Silvestre E, Meseguer-Ferrer N, et al. An outbreak of monophasic and biphasic *Salmonella* Typhimurium and *Salmonella* Derby associated with the consumption of dried pork sausage in Castellon (Spain). Enferm Infecc Microbiol Clin. 2016;34:544–50.
15. Hernández E, Santamaria R, Ramos G, Herrera-León S, Kárkamo JA, Muniozguren N. Brote de infecciones por *Salmonella enterica* serovar Typhimurium asociado al consumo de chorizo en Bizkaia. Enferm Infecc Microbiol Clin. 2016;34:577–8.
16. Yang X, Wu Q, Zhang J, Huang J, Guo W, Cai S. Prevalence and characterization of monophasic *Salmonella* serovar 1,4,[5],12:i:- of food origin in China. PLoS ONE. 2015;10:1–10.
17. Hopkins KL, Kirchner M, Guerra B, Granier SA, Lucarelli C, Porrero MC, et al. Multiresistant *Salmonella enterica* serovar 4,[5],12:i:- in Europe: a new pandemic strain? Euro Surveill. 2010;15:19580.

18. Multistate outbreak of multidrug-resistant *Salmonella* I 4,[5],12:i:- and *Salmonella* Infantis infections linked to pork (final update). http://www.cdc.gov/salmonella/pork-08-15/index.html
19. Vico JP, Rol I, Garrido V, San Roman B, Grilló MJ, Mainar-Jaime RC. Salmonellosis in finishing pigs in Spain: prevalence, antimicrobial agent susceptibilities and risk factor analysis. J Food Prot. 2011;74:1070–8.
20. Vico JP, Mainar-Jaime RC. Serological survey of *Salmonella* spp. infection in finishing pigs from northeastern Spain and associated risk factors. Span J Agric Res. 2012;10:372–82.
21. Arguello H, Carvajal A, Naharro G, Arcos M, Rodicio MR, Martín MC, et al. Sero- and genotyping of *Salmonella* in slaughter pigs, from farm to cutting plant, with a focus on the slaughter process. Int J Food Microbiol. 2013;161:44–52.