Emerging *Salmonella* 4,[5],12:i:- and antimicrobial resistance in *Salmonella* serovars isolated from swine in the Midwest

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Key Points

- Swine is the reservoir most commonly associated with the *S.4,[5],12:i:-* serotype
- The prevalence of *S. Agona* and *S. 4,[5],12:i:-* in isolates of swine origin recovered from clinical samples received at the Minnesota Veterinary Diagnostic Laboratory (MVDL) in 2006-2015 has increased
- In these serotypes an increased proportion of isolates were resistant to ceftiofur and enrofloxacin, compared with other serotypes
- The increase in the frequency of isolation of the *S.4,[5],12:i:-* serotype in humans may be paralleled by a similar increase in swine clinical samples received in the MVDL

Non-typhoidal *Salmonella* (NTS) *enterica* infections cause approximately one million human cases in the U.S. every year, with an average of 20,000 hospitalizations and 400 deaths. Most production and companion animal species can be sub-clinically infected with NTS and can therefore act as sources of infection. In addition, *S. enterica* can lead to clinical disease also in infected animals, particularly in the case of certain serotype-host species combinations such as *S.* Cholerasuis and swine. Although many of the *Salmonella* infections in humans caused by NTS are self-limiting, in some cases antimicrobial treatment is needed to prevent systemic spread of the bacteria, and thus the increasing prevalence of antimicrobial resistance (AMR) in NTS isolates from both human and animal origin in the recent years is a major concern. For this reason trends in serotypes and AMR in *Salmonella* recovered from different source (humans, animals and food) is monitored in the U.S. through the National Antimicrobial Resistance Monitoring System for Enteric Bacteria (NARMS, https://www.cdc.gov/narms/), that includes also other foodborne bacterial pathogens.

Since the late 90's the prevalence of *S. 4,[5],12:i:-,* a variant of *S.* Typhimurium that lacks the 2nd phase flagellar antigen, is increasing in the U.S. and worldwide. In the U.S.*, S. 4,[5],12:i:-* has gone from rarely reported to the 4th most common serotype among human cases in 2013 (1), and has been associated with a large number of foodborne outbreaks in the U.S. and Europe in the last 20 years. Swine is one of the potential reservoirs of NTS, and multiple serotypes have been recovered from swine samples collected in the farm and the slaughterhouse over the years at different frequencies. While considered the second most likely source of foodborne salmonellosis in Europe (2), its importance in the U.S. has been traditionally estimated to be much lower (2, 3). Still, swine is the reservoir most commonly associated with the *S.4,[5],12:i:-* serotype, since pork and pork products have been often traced as the source of human infections in several of the outbreaks caused by this serotype. Nevertheless, *S.*4,[5],12:i:- has been rarely found in pig samples collected in the slaughterhouse as part of the NARMS program (8 out of 947 samples collected between 2006-2011), so its true on-farm distribution is not known (3).

In a study conducted recently in our lab (4), a subset of approximately 2,500 NTS isolates of swine origin recovered from clinical samples received at the Minnesota Veterinary Diagnostic Laboratory (MVDL) in 2006-2015 was analyzed to assess the serotype and AMR distribution. This study confirmed that swine can be infected with a large variety of Salmonella serotypes. Serotypes Typhimurium, Derby, Agona and 4,[5],12:i:- accounted for 50% of the isolates investigated. We found that while the proportion of *S. Typhimurium* and *S. derby* isolates decreased throughout the study period, the prevalence of *S. Agona* and *S. 4,[5],12:i:-* increased (**Fig. 1**). Interestingly, those increasing serotypes (agona and 4,[5],12:i:-) showed an increased proportion of isolates resistant to ceftiofur and enrofloxacin, compared with what was found for other serotypes (4). An increase in the proportion of multidrug resistant S. 4,[5],12:i:- has been also noted in isolates from human origin (5).

These results indicates that the increase in the frequency of isolation of the *S.*4,[5],12:i:- serotype in humans may be paralleled by a similar increase in swine clinical samples received in the MVDL . This is also supported by similar findings at the Iowa State University Diagnostic Laboratory (6). The rare isolation of *S.*4,[5],12:i:- in pig samples collected at the slaughterhouses indicates that risk for public health is potentially low, but further research is needed in order to identify the factors promoting the emergence of this serotype in humans and the role that swine may play as potential reservoirs.
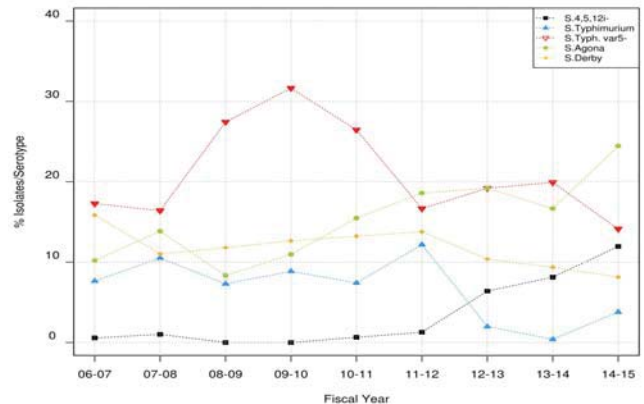

Fig. 1 –*Salmonella* **serotypes recovered from swine samples at the MVDL during 2006-2015** (percentage of isolates belonging to each serotype that were recovered each year are presented on the right axis).

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