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Review

Pre-harvest risk factors for *Salmonella enterica* in pork production☆

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ABSTRACT

Salmonella is an important issue to the pork industry worldwide. Although *Salmonella* has been identified in all links of the pork production chain, there has been increasing focus on the pre-harvest phase (on-farm). Many investigations have been conducted to identify risk factors for *Salmonella* infections in pigs. In this review, we surveyed the literature to present a compilation of the scientific knowledge currently available about potential pre-harvest risk factors for *Salmonella* infection in swine populations, and discussed some of the potential fundamental issues associated with this type of on-farm studies. Because of the dynamic relationship between the host (the pig), the agent (*Salmonella*), and the environment, definitive statements regarding transmission, shedding, and carrier states are difficult. The number of potential sources of *Salmonella* infections for a swine population is endless, and the pattern of *Salmonella* transmission and shedding in swine populations is the result of the combination of a variety of factors resulting in a multitude of potential scenarios. Pigs may be infected with *Salmonella* during any of the production stages on-farm, and as shown in this review, a variety of risk factors may affect the probability of infection. Moreover, between the farm and the abattoir, additional factors can further increase the risk of *Salmonella* infections. Therefore, at the time of slaughter, the probability of *Salmonella* infections in pigs results from the occurrence of risk factors on-farm and between the farm and slaughter. Although a variety of risk factors has been reported, the lack of consistency, the methodological limitations, as well as the complex and dynamic epidemiology of *Salmonella* in swine populations prevent definitive conclusions. Based on the evidence available at the moment, we conclude that pre-harvest *Salmonella* control programs must be based essentially on strict measures of biosecurity and hygiene, which should minimize the risk of exposure of the pigs to potential infection sources, as well as the persistence of the bacteria in the herd. Moreover, particular attention must be given to the pre-slaughter process of transportation and lairage, where rigorous washing and disinfection programs should be applied.

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Contents

1. Introduction

Salmonella is an important issue to the pork industry worldwide, because of its implications for public health and high societal costs. It is estimated that 80.3 million cases of foodborne salmonellosis occur annually in the world (Majowicz et al., 2010). In the U.S., *Salmonella* is the second leading cause of foodborne illness, and the leading cause of hospitalization and death (Scallan et al., 2011). Although the precise

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number of human salmonellosis cases directly attributable to pork or pork products is difficult to determine, reported estimates range from <1% to 25% (Berends, Van Knapen, Mossel, Burt, & Snijders, 1998; Guo et al., 2011; Hald, Vose, Wegener, & Koupeev, 2004; Miller, Liu, McNamara, & Barber, 2005).

Salmonella has become a very important food safety issue for the U.S. swine industry due to its potential impact on domestic public health and consumer confidence, as well as the need to remain competitive in the international market. As pork has gained recognition as a source of human salmonellosis, *Salmonella* surveillance and monitoring programs have been implemented in several countries, particularly in Europe (Abrahantes, Bollaerts, Aerts, Ogunsanya, & Van der Stede, 2009; Boyen et al., 2008; Snary, Munday, Arnold, & Cook, 2010). Although *Salmonella* has been identified in all links of the pork production chain, there has been increasing focus on the pre-harvest phase (i.e., on-farm). One of the greatest challenges of this approach lies in developing effective intervention measures that can be applied at the herd level. However, in order to be able to develop effective intervention measures, it is essential that risk factors for the occurrence of *Salmonella* infections in swine herds be identified. By identifying and quantifying the effects of risk factors, interventions can be developed and applied to reduce *Salmonella* infection and carriage in the pigs at the herd level, which will reduce the contamination pressure at the abattoir.

A number of studies conducted around the world have investigated potential risk factors for *Salmonella* infections in pigs. In this review, we surveyed the literature to present a compilation of the scientific knowledge currently available about potential pre-harvest risk factors for *Salmonella enterica* infection in swine populations. Furthermore, we discuss some of the potential fundamental issues associated with on-farm studies investigating the epidemiology of *S. enterica* in swine populations, particularly when attempting to identify such risk factors.

2. *Salmonella* infection in swine

Pork contamination occurs in the abattoir, along the slaughter and processing line. Incoming pigs carrying *Salmonella* in their intestinal tract increase the risk of contamination of carcasses and pork products. When a contaminated intestinal tract is lacerated, the whole carcass as well as neighboring carcasses is exposed (Baptista, Dahl, & Nielsen, 2010; Berends, Van Knapen, Snijders, & Mossel, 1997; Botteldoorn, Herman, Rijpens, & Heyndrickx, 2004; Vieira-Pinto, Tenreiro, & Martins, 2006). Therefore, it is critical to understand the dynamic of *Salmonella* infections in swine herds supplying the abattoirs.

Transmission of *Salmonella* in swine occurs mainly via the fecal–oral route (Boyen et al., 2008; Griffith, Schwartz, & Meyerholz, 2006). However, the respiratory tract constitutes a portal of entry as well (Fedorka-Cray, Kelley, Stabel, Gray, & Laufer, 1995; Proux et al., 2001). In fact, airborne transmission of *Salmonella* has been demonstrated in swine (Oliveira, Carvalho, & Garcia, 2006; Oliveira, Garcia, Carvalho, & Givisiez, 2007). *Salmonella* is able to rapidly spread through the gastrointestinal tract, being shed in the feces within only 2 h post-infection (Boughton, Egan, Kelly, Markey, & Leonard, 2007a, 2007b; Hurd, Gailey, McKean, & Rostagno, 2001; Rostagno, Eicher, & Lay, in press). However, to date, the mechanism(s) involved in the rapid dissemination of *Salmonella* in pigs is not known. The minimum disease-producing dose has not been established, but disease is difficult to reproduce experimentally. Transmission studies exposing pigs to *Salmonella* contaminated environments have shown that low numbers of the bacteria (10^2–10^3 CFU) are enough to infect the exposed animals (Boughton et al., 2007a; Fedorka-Cray, Whipp, Isaacson, Nord, & Lager, 1994; Hurd et al., 2001). Rostagno, Eicher, et al. (in press) demonstrated that finishing pigs can carry in the intestinal tract and associated lymph nodes, and excrete high numbers of *Salmonella* in feces continuously for up to 4 weeks post-infection without any clinical symptom. However, it seems that both infectious dose, and serovar are important determining factors for establishing the infection, and the amount and pattern (continuous or intermittent) of bacteria shedding (Gray, Fedorka-Cray, Stabel, & Kramer, 1996; Loynachan, Nugent, Erdman, & Harris, 2004; Osterberg, Lewerin, & Wallgren, 2009; Osterberg & Wallgren, 2008). However, further research is still required to unravel these effects.

Salmonella infections in swine herds are much more common than the clinical disease (i.e., salmonellosis). Asymptomatic intestinal carriage and intermittent shedding of *Salmonella* characterize most subclinically infected pigs, which represents a very common scenario in swine herds around the world. Pigs can potentially remain a risk to food safety for *Salmonella* long after they have been infected, excreting the bacteria in feces and/or harboring it in several tissues, particularly the intestinal tract, and associated lymph nodes (Boyen et al., 2008; Griffith et al., 2006). Pigs subjected to experimental inoculation and also under natural conditions (i.e., on-farm) have been shown to carry and intermittently shed *Salmonella* for many weeks (Kranker, Alban, Boes, & Dahl, 2003; Nielsen, Baggesen, Bager, Haugegaard, & Lind, 1995; Osterberg & Wallgren, 2008; Rostagno, Eicher, et al., in press; Scherer et al., 2008; van Winsen et al., 2001; Wood, Pospichil, & Rose, 1989).

The vast majority of *S. enterica* serovars are able to colonize the gastrointestinal tract of a range of animals (including, swine), and may cause enteritis or subclinical infections. However, *Salmonella* can also be considered as a commensal organism of the gastrointestinal tract, making difficult the differentiation between infection and carriage. As a pathogen, *Salmonella* possess the required biological properties that enable it to colonize and penetrate mucous surfaces, grow/multiply within the host, inhibit or avoid host defenses, and damage the host. However, on the other hand, *Salmonella* may also sometimes be carried by the host without causing harm or disease. For instance, Rostagno, Eicher, et al. (in press) demonstrated how finishing pigs can be challenged with a high dose of *Salmonella* Typhimurium, subsequently carrying and shedding the organism for several weeks, without any evidence of deleterious effects, including complete absence of fever. The complex in vivo behavior of *Salmonella* has been the subject of many recent studies, and it is proving to be a quite complex and fascinating area. However, in addition to the current need of further studies to increase our knowledge on the swine–*Salmonella* interactions, the subject is out of the scope of the present review.

Several on-farm studies reported discrepancies between bacteriologic and serologic *Salmonella* prevalence estimates in swine herds, with serologic estimates often higher than bacteriologic estimates (Funk, Harris, & Davies, 2005; Hurd, McKean, Griffith, & Rostagno, 2004; Lo Fo Wong et al., 2003; Stege et al., 2000). However, it is well known that a temporal disassociation exists between infection and serologic response. *Salmonella* seroconversion has been estimated to occur within 7–14 days post-infection under experimental inoculation conditions (Nielsen et al., 1995; van Winsen et al., 2001), and after a longer period in naturally occurring infections (Kranker et al., 2003). Therefore, recent *Salmonella* infections usually cannot be detected by serology. On the other hand, serologically positive pigs may not continue to shed *Salmonella* in the feces (or shed intermittently) and, therefore, would not be detected by bacteriology. Studies with experimentally infected groups of pigs have shown that the peak seroprevalence occurs at approximately 30 days post-inoculation (Nielsen et al., 1995; Srinand, Robinson, Collins, & Nagaraja, 1995; van Winsen et al., 2001; Wood et al., 1989; Wood, Rose, Coe, & Ferris, 1991). Therefore, it is not unexpected that a different pattern of bacteriologic and serologic responses may, and probably, do occur, under natural conditions. This scenario becomes even more complicated, because pigs within herds (or lots) are infected at different points in time with variability in both exposure rate and level. Moreover, the common occurrence of multiple *S. enterica* serovars within a herd (simultaneously or sequentially) will further complicate this scenario.

A variety of *S. enterica* serovars have been recovered from pigs on-farm and at slaughter. However, although wide variation of serovar distribution is observed between individual production systems, when large swine populations (e.g., regions or countries) are considered, a similar pattern emerges with a consistent predominance of serovars Typhimurium, Typhimurium var. Copenhagen, and Derby. Other commonly occurring serovars include; Anatum, Infantis, Agona, Ohio, and Brandenburg (Davies, Dalziel, et al., 2004; de Jong et al., 2009; Farzan et al., 2008; Garcia-Feliz et al., 2007; Rostagno, Hurd, & McKean, 2007; van Duijkeren, Wannet, Houwers, & van Pelt, 2002).

Because of the dynamic relationship between the host (i.e., the pig), the agent (i.e., *Salmonella*), and the environment, precise statements regarding transmission, carrier states, and shedding are very difficult. Essentially, the pattern of *Salmonella* transmission and shedding in swine populations results from the combination of an endless variety of factors leading a multitude of potential scenarios.

3. On-farm risk factors

The number of potential sources of *Salmonella* infections for a swine population is virtually endless. Epidemiological studies, based on a variety of approaches, have been conducted to determine potential risk factors for *Salmonella* infection in swine herds around the world. As presented in this review, a variety of factors have been included in these on-farm studies, including feed type, use of antibiotics, infections, herd size, hygienic practices, floor type, contact between pigs, number of pig sources, and others.

The role of feed as a potential source of *Salmonella* is well established and reviewed (Crump, Griggin, & Angulo, 2002; Davies, Hurd, et al., 2004; Molla et al., 2010). Because of that, and also because of its logical direct relation with the pigs' intestinal microbial ecology, several studies have investigated different aspects related to feed and feed management as potential risk factors for *Salmonella* infections in pigs. Numerous studies have reported an association between pelleted feed and increased risk of *Salmonella* infection in swine herds, based on bacteriologic and serologic prevalence (Farzan et al., 2006; Garcia-Feliz, Carvajal, Collazos, & Rubio, 2009; Hautekiet, Geert, Marc, & Rony, 2008; Hotes, Kemper, Traulsen, Rave, & Krieter, 2010; Kranker, Dahl, & Wingstrand, 2001; Leontides, Grafanakis, & Genigeorgis, 2003; Lo Fo Wong et al., 2004; Poljak, Dewey, Friendship, Martin, & Christensen, 2008; Rajic, Chow, et al., 2007; Rajic, O'Connor, et al., 2007; Wilkins et al., 2010). On the other hand, the use of liquid feeding has been associated with decreased risk of *Salmonella* infection in swine herds, in comparison to solid feed (Hotes et al., 2010; Poljak et al., 2008; van der Wolf et al., 1999). Furthermore, the use of fermented liquid feeding or liquid feeding with fermented byproducts has also been associated with low bacteriologic and serologic *Salmonella* prevalence (van der Wolf et al., 1999, 2001). Additionally, according to several studies (Bahnson, Fedorka-Cray, Ladely, & Mateus-Pinilla, 2006; Beloeil, Fravalo, et al., 2004; Dahl, 1997; Farzan et al., 2006; Hautekiet et al., 2008; Leontides et al., 2003), the use of wet feed was associated with lower bacteriologic and serologic *Salmonella* prevalence than in swine herds using dry feed. However, Rajic, O'Connor, et al. (2007) reported the opposite finding, with herds using wet feed actually having higher bacteriologic *Salmonella* prevalence than herds using dry feed.

Feed constitutes the nutritional substrate for both the pigs and their gastrointestinal microbial ecosystem. Changes in feed physical structure and composition affect gastric passage and intestinal transit, leading to changes in osmolarity, pH, and mucin production, which in turn affect a variety of physiologic and metabolic processes within the gastrointestinal tract, including microbial populations. For instance, it has been shown that pelleted feed decreases stomach acidity (i.e., increases pH) compared to coarse feed, in addition to increasing mucin secretion, contributing to the survival of ingested *Salmonella* and colonization of the pig (Hedemann, Mikkelsen, Naughton, & Jensen, 2005; Mikkelsen, Naughton, Hedemann, & Jensen, 2004). On the other hand, the use of liquid feeding (particularly, fermented) decreases pH and favors selected microbial populations in the gastrointestinal tract creating a hostile environment for *Salmonella* survival and colonization (Hotes et al., 2010).

Another factor potentially associated with *Salmonella* infections in swine herds is the use of antibiotics. However, due to a variety of potential confounding factors related to the intestinal microbial ecology in the host (i.e., the pigs), the susceptibility/resistance characteristics of the *Salmonella* strain present (or introduced) in the herd, and also to the dose and route of administration of the drugs, reported results are usually inconsistent, particularly when trying to determine the potential role of specific antibiotics as risk factor for *Salmonella* (Beloeil et al., 2007; Farzan et al., 2006; Funk et al., 2007; Funk, LeJeune, Wittum, & Rajala-Schultz, 2006; Hotes et al., 2010; Leontides et al., 2003; Rajic, Chow, et al., 2007; van der Wolf et al., 2001). On-farm antibiotic use is only one factor affecting bacterial resistance, which is also affected by several other on-farm factors that also influence the emergence of resistant foodborne pathogens, such as *Salmonella* (Farzan, Friendship, Dewey, Poppe, & Funk, 2010; Varga, Rajic, McFall, Reid-Smith, & McEwen, 2009). Nevertheless, this is a very important area that still needs to be explored. Recent studies investigating the prevalence of *Salmonella* in antibiotic-free versus conventional pork production systems (i.e., with regular use of antibiotics) have reported inconsistent results. Gebreyes, Thakur, and Morrow (2006); Gebreyes, Bahnson, Funk, McKean, and Patchanee (2008) reported significantly higher bacteriologic and serologic *Salmonella* prevalence in antibiotic-free herds compared to conventional herds, with an odds ratio of 4.23. In contrast, Thakur et al. (2007) reported a significantly higher *Salmonella* prevalence in pigs from conventional than in pigs from antibiotic-free production systems. The antibiotic resistance profile of foodborne pathogens isolated from conventional and antimicrobial-free production systems has also been investigated. For instance, Gebreyes et al. (2006) reported that *Salmonella* isolated from conventional herds were more frequently resistant to most classes of antibiotics compared to *Salmonella* isolated from antimicrobial-free herds; isolates from conventional herds were also more likely to be resistant to multiple antibiotics. However, it is also important to note that antibiotic-resistant strains were also isolated from antibiotic-free herds, but less frequently. This observation illustrates the complex and widespread nature of antibiotic resistance. While it is clear that not using antibiotic in pig production results in fewer antibiotic-resistant bacteria in the pig, there are currently very few studies examining whether these reductions result in fewer antibiotic-resistant bacteria (including, *Salmonella*) on the final pork and pork products. This type of investigation is very complex and difficult to conduct, particularly due to the large number of contamination sources and confounders. Carcass contamination essentially results not only from the carriage of pathogens by the pig itself, but also from contact with other contaminated carcasses and/or surfaces in the abattoir. Hygiene varies between abattoirs and has been shown to have an important impact on carcass contamination (Baptista et al., 2010; Botteldoorn et al., 2004; Delhalle et al., 2008; Eblen et al., 2006), in addition to pre-slaughter transportation and lairage/holding, which have been shown to increase the contamination risk of the abattoir's slaughter and processing lines (Hurd et al., 2002; Rostagno et al., 2003).

A previous diagnosis of clinical *Salmonella* infection (enteric salmonellosis or enterocolitis) in the herd has been associated with a higher *Salmonella* bacteriologic and serologic prevalence at slaughter (Oliveira et al., 2005; van der Wolf et al., 2001). Also, other infections have been experimentally shown to favor *Salmonella* infection in pigs, such as *Lawsonia intracellularis* (Moller et al., 1998) and porcine reproductive and respiratory syndrome virus (Wills et al., 2000). In a field study, Beloeil, Fravalo, et al. (2004) observed that seroconversion for *L. intracellularis* or for porcine reproductive and respiratory syndrome virus was associated with *Salmonella* shedding in finishing pigs. Moreover, Beloeil et al. (2007) reported that seropositivity for porcine reproductive and respiratory syndrome virus was associated with a 1.6 (95% CI 1.1–2.5%) increased odds ratio for *Salmonella* seroconversion. Under experimental conditions, parasite infestation has also been shown to favor *Salmonella* infection and shedding in pigs (Steenhard et al., 2002). Under natural conditions, van der Wolf et al. (2001) reported that herds with more than 16% of the livers of their market pigs condemned at slaughter as a result of white spots were associated with a higher *Salmonella* seroprevalence.

According to van der Wolf et al. (2001), small herd size was associated with high *Salmonella* seroprevalence. This observation contrasts with other studies, which found either an increasing prevalence or no difference with increasing herd size (Carstensen & Christensen, 1998; Farzan et al., 2006; Mousing et al., 1997). However, according to Garcia-Feliz et al. (2009), the odds ratio of a farm being *Salmonella*-positive was associated with its size; finishing units harvesting more than 3500 pigs per year had a higher risk for *Salmonella* shedding (OR = 1.78; 95% CI 0.96–3.31). In a study conducted by Beloeil et al. (2007), large finishing batch size was identified as a risk factor for *Salmonella* seroconversion. Rajic, O'Connor, et al. (2007) reported that finishing barns at multisite operations or individual grow-to-finish farms had a greater risk of the presence of *Salmonella* compared to finishing barns at farrow-to-finish farms.

Curiously, in a study reported by van der Wolf et al. (2001), the omission of disinfection after pressure washing a compartment as part of an all-in/all-out procedure was associated with a lower *Salmonella* seroprevalence compared to herds that sometimes or always applied disinfection. Moreover, Poljak et al. (2008) observed that increased frequency of disinfection and washing with cold water was positively associated with *Salmonella* shedding; in the same study, completely closed barns were associated with lower *Salmonella* shedding prevalence. But, according to Farzan et al. (2006), herds applying a continuous flow system (instead of all-in/all-out) had increased risk of having *Salmonella*-positive pigs (OR = 2.3; 95% CI 1.2–12.7). According to Lo Fo Wong et al. (2004), pigs produced in herds with hygienic facilities (i.e., locker room for employees) had more than three times lower odds of being seropositive compared to pigs in herds with no such facilities. Moreover, in the same study, herds where the caretaker washed hands consistently had one and a half lower odds of seropositivity than herds where the caretaker did not. Rajic, O'Connor, et al. (2007) observed that farms requiring their personnel or visitors to shower before entering and before leaving had increased odds of the presence of *Salmonella* compared with farms that provided boots and coveralls; no significant difference was observed between the latter category and farms that used boot disinfection. Hotes et al. (2010) also observed that the use of protective clothing and even irregular cleaning of the feed tube reduced the chance of a *Salmonella*-positive pig. The biosecurity measures of wearing specific clothes before entering the facilities and enclosing the pig farm facilities were also protective in a study conducted by Beloeil et al. (2007). These reports underscore the importance of humans (particularly, farm workers) as contributors for the transmission of *Salmonella* in the herds.

According to Davies et al. (1997), housing finishing pigs on solid concrete floors with open-flush gutters increases the risk of *Salmonella* shedding compared with housing on slotted concrete floors. More recently, Nollet et al. (2004) and Hotes et al. (2010) reported that type of floor was related to *Salmonella* prevalence. According to these studies, herds with fully slotted floors had lower bacteriologic and serologic prevalence. Moreover, emptying the pit below the slotted floor after a batch of sows was removed and frequent removal of sow dung during the lactation period was associated with lower frequency of *Salmonella*-positive pigs in farrow-to-finish herds (Beloeil, Fravalo, et al., 2004). Additionally, in the same study, occurrence of residual *Salmonella* contamination of the floor and pen partitions in the finishing rooms before housing the growing pigs was also a risk factor for infection. Environmental contamination after cleaning and disinfection of finishing pens was also reported by Funk et al. (2001) as a common occurrence in *Salmonella* positive herds. In a study conducted by Beloeil et al. (2007), the presence of residual *Salmonella* contamination in the finishing pen before placing the pigs into the pens had an odds ratio of 1.9 (95% CI 1.2–2.9) for *Salmonella* seroconversion.

According to Lo Fo Wong et al. (2004), pigs that were able to have snout contact with pigs in neighboring pens (due to open or low pen separations) had a higher chance of being seropositive compared to pigs with no such contact. Also, in a study conducted by Wilkins et al. (2010), nose-to-nose pig contact through pens was associated with increased *Salmonella* prevalence.

Lo Fo Wong et al. (2004) observed that pigs in herds with more than three suppliers had three times higher odds of being seropositive than pigs in herds that bred their own replacement stock or with a maximum of three suppliers. Later, Zheng et al. (2007) reported that the proportion of seropositive pigs in the herds was mostly associated to the risk of introducing *Salmonella* in the herds by purchase and transport of growing pigs, while integrated herds were less likely to become infected.

A variety of additional risk factors may affect the probability of *Salmonella* infection of finishing pigs. For instance, according to Bahnson et al. (2006), pigs from herds with at least some bowl drinkers had eight times higher odds of testing positive for *Salmonella* than pigs from herds with only nipple drinkers. Also, the breeding herd has been shown to be an important source of *Salmonella* persistence within farrow-to-finish farms (Wilkins et al., 2010). Moreover, proximity to other swine herds (<2 km) had odds ratio of 3.76 (95% CI 2.47–5.73) for being *Salmonella*-positive, in a study conducted by Hotes et al. (2010). Common management practices have also been shown to be capable of affecting the risk of *Salmonella* infection in finishing pigs. For example, Rostagno et al. (2009) showed that the practice of split marketing increases the bacteriologic and serologic prevalence of *Salmonella* from the first to the last group of pigs moved out of the finishing barns, immediately prior to shipping to the abattoir.

4. From the farm to the abattoir

Pigs may be infected with *Salmonella* during any of the production stages on-farm, and as shown, a variety of risk factors may affect the probability of infection. In fact, market pigs carrying *Salmonella* when leaving the production farm constitute the original source of *Salmonella* found in the abattoir. However, between the farm and the abattoir, a variety of additional factors can further increase the risk of *Salmonella* infection of live pigs, and consequently, the risk of contaminations along the slaughter and processing line.

Several studies have shown that the proportion of pigs infected with *Salmonella* increases between the farm and the abattoir (Beloeil, Chauvin, et al., 2004; Gebreyes et al., 2004; Hurd et al., 2002). These observations reveal an effect of the pre-slaughter process, which includes handling, transportation, and lairage. Each one of these steps can per se be considered as multifactorial effectors that result in increased risk of *Salmonella* contamination of pork and pork products. Consequently, consistent correlations between *Salmonella* status before shipment to slaughter (i.e., on-farm) and after entering the slaughter line (i.e., at the abattoir) are difficult to establish.

There is increasing evidence showing that stress can affect food safety risk through a variety of potential mechanisms. During the process of being transported from the production farm to the abattoir, pigs are exposed to a variety of potential stressors before slaughter (Averos et al., 2008; Warriss, 2003). As a consequence, the proportion of pigs carrying and shedding *Salmonella*, as well as the levels of the bacteria in the intestinal tract may increase in response to stressors (Rostagno, 2009).

The exposure of pigs to *Salmonella* during transportation and lairage constitutes a major risk factor for infection immediately before slaughter. Presence of *Salmonella* in transportation trailers prior to loading pigs at the farm has been shown to be common by several studies (Gebreyes et al., 2004; Mannion et al., 2008; Rajkowski et al., 1998). Additionally, lairage has been shown to be a major source of *Salmonella* infection for pigs entering the slaughter and processing line (Boughton et al., 2007b; De Busser et al., 2011; Dorr et al., 2009; Rostagno et al., 2003; Swanenburg et al., 2001). In the end, samples collected from pigs at slaughter may contain *Salmonella* originating from the farm, from the transport trailer, and from lairage pens. Therefore, it is reasonable to conclude that samples collected at slaughter provide a composite of farm, transport and lairage risk factors.

5. Investigation of on-farm risk factors: Some critical issues to consider

While reviewing the epidemiological studies on risk factors for *Salmonella* infections in pigs available in the literature, it became evident that there are several issues to be considered across different studies. For instance, differences and inconsistencies between reports can be caused by the place of sampling (farm or abattoir), sampling design (sample size and selection, and type of sample), and diagnostic approach (bacteriologic culture or serologic detection). Of particular relevance is the observed multitude of bacteriologic and serologic methods applied in the studies included in this review. It is well known that considerable differences exist regarding the performance (e.g., sensitivity and specificity) of different diagnostic methods.

The effective identification and evaluation of risk factors as well as the development and implementation of reliable pre-harvest monitoring and control programs depend on the ability to accurately assess the *Salmonella* status of pig groups or populations. However, the diagnostic tools currently available for pre-harvest investigations of *Salmonella* are limited. Bacteriologic culture is labor intensive and time consuming, and it has been shown to have low to moderate sensitivity (Funk et al., 2000, 2005; Hurd et al., 2004). On the other hand, although serologic detection allows testing a large number of samples rapidly and at relatively low cost, considering that the presence of antibodies reflects previous exposure to *Salmonella* rather than current infection, the relationship between serologic status and microbial risk is less evident than with bacteriologic culture. Additional issues regarding the dynamics of *Salmonella* infection and transmission in swine herds were previously discussed in this review.

It is also important to keep in mind that epidemiologic aspects of *Salmonella* infections in swine herds as well as the impact and feasibility of interventions may not be directly transferable between different countries (or even between different production systems within the same country), due to differences in production systems and industry structure. Pork production systems differ substantially among countries. Therefore, it is important to mention that studies included in this review were conducted in several different countries (e.g., The Netherlands, Greece, Belgium, Denmark, France, United States, Canada, and Spain), and in different types of production farms (e.g., farrow-to-finish systems, integrated production systems, and multiple and individual finishing sites). The heterogeneity of pork production systems and likely confounding of potential risk factors, very likely impact results of epidemiological studies, which therefore, should be interpreted cautiously.

In fact, Sanchez et al. (2007) reported results of a systematic review and meta-analysis study aiming at identifying variables causing between-study variation in *Salmonella* prevalence estimates. In this study, diagnostic procedure, sample size, country, and sampling design were some of the most important predictors in explaining the differences in *Salmonella* prevalence observed between studies. These findings support the previous considerations presented.

Recent epidemiological studies have shown that *Salmonella* prevalence in swine populations is very dynamic, changing over time, and between cohorts (Rajic, Chow, et al., 2007; Rostagno, Hurd, & McKean, in press). Therefore, longitudinal sampling and testing are required to properly evaluate on-farm *Salmonella* status. As a consequence, the cross-sectional design approach commonly applied in epidemiological surveys to identify risk factors for *Salmonella* infection in swine herds warrants some consideration. As the infection status of the animals and the potential risk factors are determined at a particular time point, cross-sectional studies are best suited to identify factors that are constant over time, and not influenced by presence or absence of infection. Moreover, variables or factors not included in the study, but associated with the prevalence of *Salmonella* will result in significant confounding effect. Therefore, in cross-sectional surveys, causality between risk factor(s) and the outcome (*Salmonella* infection) is sometimes difficult to assess. Nevertheless, cross-sectional surveys should be considered as valuable exploratory studies to identify potential risk factor(s), which should be further investigated through prospective studies or specifically designed experiments accounting for these issues.

6. Conclusions

The incidence of *Salmonella* in pork can be reduced, based on different approaches. Intervention measures can be applied pre-harvest (i.e., on-farm), post-harvest (i.e., at the abattoir), or both. Although a variety of intervention measures to reduce the risk of carcass contamination are routinely applied along the slaughter and processing lines at the abattoirs, additional measures can be adopted (e.g., separate or sanitary slaughter, and carcass wash or decontamination). However, it is generally accepted that controlling *Salmonella* at the farm level would have a major impact by reducing the contamination pressure constantly entering the abattoirs, which would potentially increase the efficiency of the post-harvest contamination control measures. In fact, experience from the Danish surveillance and control program for *Salmonella* in pigs and pork shows that a combination of pre- and post-harvest measures is critical to effectively reduce the incidence of *Salmonella* in pork (Alban et al., in press; Wegener, 2010).

In order to develop effective intervention measures and control *Salmonella* in the pre-harvest pork production chain (i.e., on-farm), it is necessary, first, to identify the most important risk factors. However, further research is still necessary to better understand, and evaluate the association between the risk factors reported in the literature and *Salmonella* infection in swine herds. Although a variety of risk factors has been reported, the lack of consistency, the methodological limitations, as well as the complex and dynamic epidemiology of *Salmonella* in swine populations prevent definitive conclusions. Therefore, the on-farm control of *Salmonella* in swine herds continues to be difficult, which constitutes a persistent challenge to the pork production industry worldwide. Based on the evidence available at the moment, we conclude that pre-harvest *Salmonella* control programs must be based essentially on strict measures of biosecurity and hygiene, which should minimize the risk of exposure of the pigs to potential infection sources, as well as the persistence of the bacteria in the herd. Moreover, particular attention must be given to the pre-slaughter process of transportation and lairage, where rigorous washing and disinfection programs should be applied.

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