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Vaccination against *Streptococcus suis*: Effect on nursery mortality

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Summary

Purpose: To evaluate the effect of selected vaccines and administration routes on mortality of nursery pigs due to *Streptococcus suis*.

Methods: A field trial was conducted on one group of nursery pigs (N=330). Pigs were randomly allocated to one of four groups that each received one of the following treatments at weaning: an experimental autogenous vaccine administered intramuscularly (IM) (n = 90); a standard autogenous vaccine administered IM (n = 90); a commercial bacterin, administered intraperitoneally (IP) (n = 60); or no vaccine (n = 90). Nursery mortality was monitored from the start of the trial (18 days of age) until the end of the nursery period (9 weeks of age).

Results: Nursery mortality before the start of the trial was approximately 17%. There were no significant differences among the four treatment groups; however, there was a trend toward decreased mortality among pigs that received the experimental autogenous vaccine. Overall nursery mortality at the end of the trial had decreased to 3.3%. Following the trial, an IP vaccination protocol with the commercial bacterin was initiated among all nursery pigs for 6 months. Total nursery mortality while this protocol was in place was 3.48% (SD = 1.45) and the mortality rate for pigs that showed CNS signs at the time of death was 2.55% (SD = 1.2). After this 6-month vaccination program, the owner of the herd switched to a sow vaccination strategy with the commercial bacterin. For the 6 months during which the sow vaccination protocol was monitored, total nursery mortality was 2.66% (SD = 1.65), with mortality of pigs demonstrating terminal CNS signs at 2.0% (SD = 1.61).

Implications: Vaccination does not totally control *S. suis*.

Keywords: swine, *Streptococcus suis*, vaccine, mortality

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Meningitis caused by *Streptococcus suis* is becoming a more severe and uncontrollable problem in the United States swine industry. Nursery pigs are the most commonly affected, but outbreaks in finishing pigs have also been reported.[1] Mortality rates of 4%–5% are common, and can increase to 15%. It is not clear why *S. suis* infections are increasing in prevalence, but it could be associated with:

- early weaning systems, in which pigs are weaned at ≤18 days of age,[2]
- herds that have recently enlarged their sow inventory, and
- concurrent infections that may be present in the herd, such as porcine respiratory and reproductive virus (PRRSV).[3]

Different measures to control meningitis—including intensive antibiotic treatments and/or vaccination of the piglets or the sows—have been attempted, but have not been successful.[4] Several commercial and autogenous *S. suis* vaccines are available, but their field effectiveness has not been reported. Although they do not seem to achieve total control of the problem, vaccine use has been reported to decrease mortality to more manageable levels.[5]

Previous work has suggested that the early stages in the pathogenesis of *S. suis* may involve dissemination of the bacteria surviving within macrophages.[6] This suggests that protection may depend on stimulating cellular immunity — something that is unlikely to happen with killed vaccines using conventional adjuvants and injection routes.[7,8] The IP route has been reported to give better stimulation of both humoral and cellular immune responses.[8] This paper reports our study of the effects of oil-adjuvanted IP vaccination against *S. suis*.

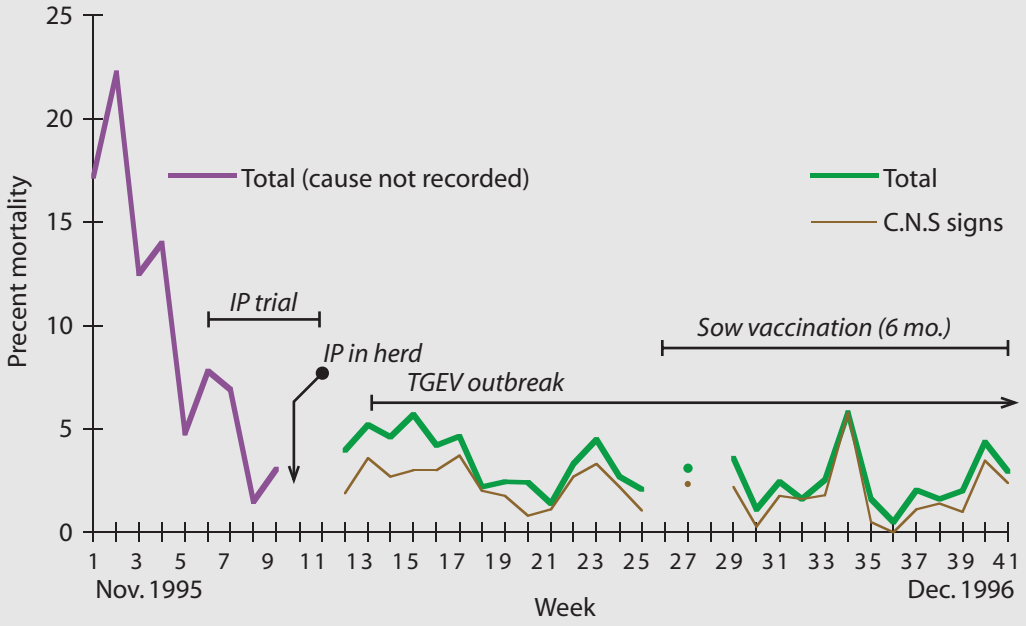
Material and methods

Herd history and clinical evaluation

In October 1995, the owners of a commercial swine herd contacted the University of Minnesota and reported high levels of nursery mortality (Figure 1). This herd was established at the beginning of 1994, but its target sow inventory (975 sows) was not reached until mid-1995. The herd was a two-site production unit with farrowing and nursery rooms at one site and finishers at another site. The average weaning age was 15 days, with preweaning mortality of 11% and average sow parity of 2.0. Replacement gilts were selected from the finishing herd and only boars were purchased from outside.

The herd had elevated nursery mortality rates in September 1995 that reached 17%. All affected pigs showed signs of meningitis, arthritis, or a

Figure 1



Nursery mortalities from November 1995 through December 1996
IP trial: Results from the group of pigs in which the vaccination trial was conducted
IP in herd: First group of pigs that had gone through the IP vaccination performed in the herd
TGEV outbreak: Prior to the outbreak, mortality was not distinguished between CNS and other causes
Sow vaccination: Results from the first group of pigs that came from vaccinated sows

combination of these signs. *Streptococcus suis* serotype 2 was isolated from the brain samples of 12 necropsied pigs submitted at different times to a diagnostic laboratory. Most of the mortality occurred between 3 and 7 weeks after weaning. Clinically affected pigs were injected with ampicillin and/or ceftiofur sodium and put into a sick pen.

During the course of the present study, this herd was concurrently infected with PRRSV and transmissible gastroenteritis virus (TGEV). A clinical PRRSV outbreak was observed in January 1996, but serology performed in March 1995 had already shown some seropositive pigs. A TGEV outbreak was clinically observed in March 1996 and affected mostly baby and nursery pigs, but no virus isolation was performed.

Field vaccine trial

In consultation with the herd owner, a *S. suis* vaccination program was initiated in November 1995. Because the literature reports inconsistent findings regarding the efficacy of the *S. suis* vaccines,[4,5,9] we performed a concurrent controlled study in the herd with pigs from only 1 week of production.

One weekly group (330 pigs) of 15-day-old pigs was randomly distributed into four experimental groups, and allocated to a 12-pen room at weaning. Each pen housed 30 pigs, with one empty pen used as a sick pen. All pigs were housed in the same room, but pens had solid partitions between them and no pigs were moved other than to house them in the sick pen at one end of the same room. Each treatment group (three pens of 30 pigs each) received one of the following treatments:

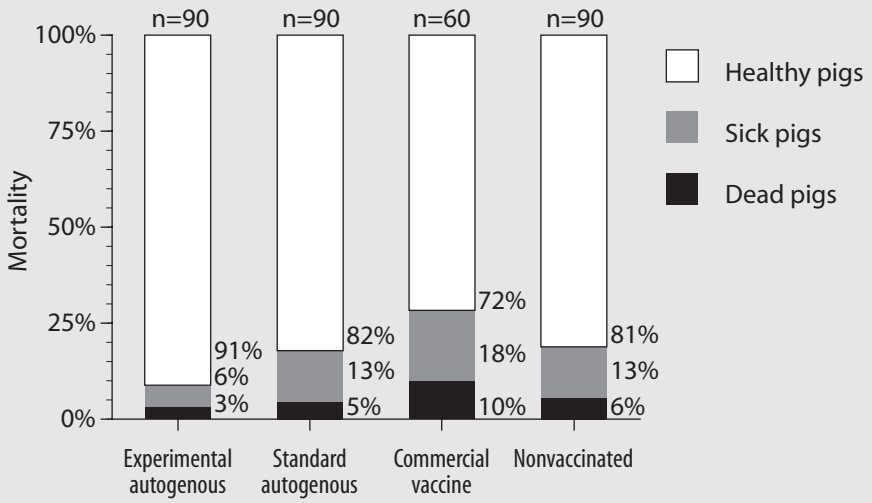
- An experimental autogenous vaccine prepared in our laboratory using the *S. suis* serotype 2 isolated from the brain of a neurologically affected pig in the herd (n = 90). This vaccine had an oil-in-water adjuvant (Imugen®, Bayer Animal Health, Worthington, Minnesota), adjusted at 4×10^8 CFU per mL, inactivated with 0.2% formaldehyde, and administered intraperitoneally (IP).
- An autogenous vaccine that was commercially prepared with a serotype-2 isolate recovered from brain tissue from the herd 10 months previous to the trial (n = 90). It had an aluminium hydroxide adjuvant and was administered intramuscularly (IM).
- A commercial bacterin prepared with a serotype-2 strain, oil-in-water adjuvant, administered IP (manufacturer recommendations suggest IM administration) (n = 60).
- nonvaccinated controls (n = 90).

Pigs were vaccinated at weaning and revaccinated 10 days later. Pigs with signs of meningitis and/or arthritis were placed in the sick pen and injected with ampicillin (6–8 mg per kg) or ceftiofur sodium (3–5 mg per kg). Morbidity and mortality rate was monitored from the beginning of the trial (at weaning) until the pigs left the nursery (at 9 weeks of age).

Statistical analysis

Differences in morbidity and mortality between groups were statistically analyzed using the χ-square test. Groups were considered to be statistically significant at $P < .05$.

Figure 2



Results of the experimental vaccination trial against *Streptococcus suis*
P value between treatments:

Association	*P* value
Experimental autogenous × standard autogenous	*P* = .08
Experimental autogenous × commercial vaccine	*P* = .02
Experimental autogenous × nonvaccinated controls	*P* = .08
Standard autogenous × commercial vaccine	*P* = .41
Standard autogenous × nonvaccinated control	*P* = 1.0
Commercial vaccine × nonvaccinated control	*P* = .41

Posttrial vaccination protocols

Following this controlled trial, the producer adopted a new vaccination protocol that was designed to boost the immune response and protect pigs with different levels of maternal immunity. Starting in late November 1995, piglets were vaccinated with the commercial bacterin IP at 5 days of age, revaccinated IP at weaning (15 days of age), and revaccinated again 10 days later IM. This program was followed in the herd for 6 months.

A TGEV outbreak in March 1996 convinced the producer to begin attempts to determine the causes of nursery pig mortality. Thus, after March 1996, the herd records differentiated between total mortality data of pigs and mortality that could be directly attributed to *S. suis* (i.e., pigs that exhibited obvious CNS distress, ataxia, tremors, and paddling).

In May 1996, the producer decided to adopt a sow vaccination protocol, which was less expensive, less time consuming, and easier to implement. Sows were vaccinated IM with the commercial bacterin at approximately days 77 and 98 of gestation. Piglets were followed during the nursery stage, and mortality rates were used to evaluate the effectiveness of this protocol. This protocol was still in use at the time of this report.

Results

Pigs that received the experimental autogenous vaccine tended to have lower morbidity/mortality ($P < .1$) than pigs in the other groups (Figure 2). Mortality in the nonvaccinated group was 5.5 % and morbidity was 13%; both were lower than the 17% mortality observed in groups of weaned pigs in the herd previous to the on-farm vaccine trial. Mortality was nonexistent among pigs vaccinated with the commercial vaccine during the first 4 weeks of the experiment, but increased to 10% during the last 2 weeks of the trial.

In comparison, mortality rate was 14% for a nearly identical group of pigs that was not vaccinated and that received identical diet and management and was weaned within 1 week of the pigs included in the trial. These pigs were housed in an adjacent room to those included in the trial, and shared the same airspace.

After the trial, when the IP vaccination protocol was initiated for all nursery pigs in the herd (n = 22 weekly groups), mortality for the nursery pigs averaged 3.48% (SD = 1.45) and the average mortality of pigs exhibiting terminal CNS signs was 2.55% (SD = 1.2). Pigs showed inappetance for 1 day after vaccination. In addition, small (approximately 2 mm in diameter) focal lesions of peritonitis were observed in some of the nursery pigs that died during the nursery stage. These lesions had not been observed during the previous experimental vaccination trial, in which the IP vaccination was performed on older pigs. None of the nursery pigs that received the IP commercial bacterin subsequent to the field trial were condemned at slaughter, suggesting that the lesions had either resolved or were not significant.

Total mortality of nursery pigs during the sow vaccination protocol was 2.66% (SD = 1.65) (n = 26 weekly groups of pigs) and mortality of the pigs that died with terminal CNS signs was 2.0% (SD = 1.61) (n = 26 weekly groups of pigs).

Discussion

It is always difficult to assess observations made in field trials, because there are many uncontrolled factors in commercial herds that can influence the results. Therefore, the effect of vaccination in reducing mortality of nursery pigs attributable to *S. suis* in this trial cannot be definitively assessed. It is tempting to attribute the decrease in mortality rates to the vaccine, but because other factors in the herd—which might have had effects on mortality—were not controlled, it is impossible to make definite conclusions about the role of vaccine in this herd.

Nursery mortalities were already decreasing at the time the experiment was begun (Figure 1). The fact that mortality for the trial pigs was lower than both the previous and succeeding groups of pigs from that nursery room suggest that the vaccine may have been somewhat efficacious in reducing morbidity and mortality due to *S. suis* in this herd. The nonvaccinated group that served as a control in the field trial had lower morbidity and mortality than expected based on previous morbidity and mortality rates in the herd. If the morbidity and mortality rates for the nonvaccinated controls had remained at 17%, the difference between this group and vaccinated groups would probably be statistically significant. The reduced morbidity and mortality rates observed in the nonvaccinated control pigs is not uncommon in field trials and could be attributable to decreased challenge exposure from the vaccinated pigs in the same room.

Because the role of maternal immunity in *S. suis* infections is unknown and because we can only estimate when colonization by the virulent strain occurs,[10] we decided to be conservative and vaccinate the piglets IP at 5 days of age, with revaccination at weaning and 10 days later. This extensive vaccination protocol was designed to give increased coverage to those pigs that might be receiving the first vaccine dose while still under maternal protection.

Mortality was being kept at reasonable levels when the outbreak of TGEV took place (May 1996). This outbreak also shows that even though the herd was a two-site, high-health facility, its biosecurity was not tight. Nursery mortalities increased during the TGEV outbreak, making it difficult to differentiate mortality due to *S. suis* from mortality caused by the TGEV. During the outbreak, there were groups with very high mortality (5%) together with groups with very low mortality (1.4%). It is not uncommon to observe variability in the mortality due to *S. suis* between groups from consecutive weaning weeks. This is often attributed to variation in the weather, temperature, or humidity as well as other factors, but no studies have been done to support this conjecture.[11]

We observed a decrease in nursery mortality after the sow vaccination protocol was initiated when the first close-outs of pigs coming from vaccinated sows were evaluated. It is worth noting that every time a change was implemented in the herd, an improvement was observed regardless of treatment. However, after several groups of pigs had gone through after the sow vaccination protocol was begun, mortality increased again and fluctuated as before. Both total mortality and CNS mortality were lower after the initiation of the sow vaccination protocol than the values observed in the vaccination trial, but the standard deviations were larger, indicating substantial variability. Although overall mortality was reduced, some groups had mortality rates as high as 5.8% (Figure 1).

It is unclear why vaccines against *S. suis* do not, in general, achieve total control of the disease. It is believed that *S. suis* reaches the brain inside monocytes, thus escaping the action of the immune system.[12] Virulent strains of *S. suis* can survive inside monocytes and multiply.[6] In theory, therefore, antibodies against *S. suis* cannot penetrate the cells and inactivate the microorganism. This would support the idea that stimulating cellular immunity would be more efficient than stimulating a humoral response to control *S. suis* meningitis. However, stimulation of cellular immunity is unlikely to occur with killed vaccines using conventional adjuvants and injection routes.[7] To address this issue, we proposed IP vaccination with an oil-in-water adjuvant as a possible strategy to stimulate a better response.[8] The results showed that although these vaccines did perform better than the conventional gel-adjuvanted IM products, they still failed to achieve complete control of the problem.

Other problems with vaccination against *S. suis* exist. The level of cross protection among serotypes is not known, but is believed to be low.[5] Membrane protein or hemolysin preparations have produced good results experimentally, but when these preparations are used in commercial herds they do not fully control the problem.[9,13,14] Because of this lack of knowledge about the virulence factors for *S. suis*, autogenous vaccines prepared with oil-in-water adjuvants seem to be, at this point, the best choice since they presumably offer a degree of cellular immune stimulation. We chose to use a commercial vaccine in the modified IP and sow vaccination program because the strain involved was a serotype 2, which is the one commonly used in commercial products.

Implications

- Vaccination against *S.suis* may help lower nursery mortalities to more manageable levels; however, this does not always totally solve the problem.
- Sow vaccination should be evaluated further, since it may give slightly better results and is less costly and labor intensive.
- The IP injection route should be considered as a possible vaccination route. However, we observed some undesirable side effects, such as peritonitis, especially in very young pigs.
- Mortality and morbidity rates in nursery pigs fluctuate regardless of treatment.

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