An evaluation of the components of medicated early weaning

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Summary: The purpose of this study was to determine which, if any, of five medicated early weaning (MEW) methods would prevent the transmission of various pathogens from dams to pigs. All animals in the study were taken from a source herd from which numerous pathogens were identified directly or by serologic tests. We randomly assigned 60 pregnant dams to one of six groups: dams in groups 1 and 2 received multiple vaccines 5 and 3 weeks prefarrowing, dams in groups 3, 5, and 6 received the conventional vaccines used by the farm 5 and 3 weeks prefarrowing, and dams in group 4 received the conventional on-farm vaccines 5 and 3 weeks prefarrowing plus oral medication 1 week prefarrowing and 1 week postfarrowing. Their offspring were randomly assigned to one of three subgroups: a subgroup (10 pigs) that was weaned at 7 days old, a subgroup (10 pigs) that was weaned at 14 days old, and a subgroup (10 pigs) that was weaned at 21 days old. All pigs were processed (i.e., received IM injections of iron dextran and procaine penicillin G, tails and canine teeth were clipped, and males were castrated) within 24 hours of birth. Each subgroup included one pig from each of the 10 dams randomized to that group. All pigs but those in group 6 were housed in isolation facilities. Pigs in group 1 and group 3 received multiple medications before and after weaning. Pigs in group 4 received oral medications before and after weaning. Pigs in group 2, 5, and 6 were not medicated. We formed three additional subgroups of barrows, two from each of the litters in groups 1, 4, and 5. These retained barrows were weaned at 7 days and placed in isolation for further testing. Except for group 6 pigs and the retained barrow subgroups, all pigs were euthanized and necropsied after 10 days in isolation rooms. Pigs from group 6 were necropsied 3 rather than 10 days after weaning. Whatever the treatment or age at weaning, Streptococcus suis was isolated from pigs in all groups. Haemophilus parasuis was not detected in the respiratory tracts of pigs in group 1 weaned at 7 and 14 days and pigs in group 3 weaned at 7 and 21 days. Bordetella bronchiseptica, a nontoxigenic Pasteurella multocida, and Mycoplasma hyopneumoniae were detected in the respiratory system of one pig, each from a different treatment and age group. Pseudorabies virus was not detected. Porcine reproductive and respiratory syndrome virus was isolated from serum of the barrows or the barrows had seroconverted in 2 of 3 groups at 42 or 64 days. In pigs subjected to medicated early weaning procedures a majority of pathogens were not transmitted. Isolating pigs was as effective (except for H. parasuis) as medication and vaccination protocols in controlling the transmission of pathogens we investigated.

Developing high-health-status pigs has been important to the swine industry for many years. In the 1950s, the specific-pathogen-free (SPF) program was developed in an effort to reduce the spread of infectious agents within and among herds, and to enable owners to sell pigs at a premium. Because of the initial expense, the uncertain benefit:cost ratio, and the possible cost of repopulation if herds became reinfected, producers have been slow to implement high-health-status programs until the results of more recent research on medicated early weaning (MEW) methods, isowean method, and all-in/all-out rearing became available.

MEW programs combine various vaccins and medications for dams and pigs, wean pigs early, and segregate pigs of various ages during rearing. These programs have been used to mingle multi-source pigs for genetic evaluation and to develop high-health-status pigs.

MEW protocols such as those devised by Alexander et al., Meszaros et al., Connor, and Wiseman are relatively expensive; however, medication (one of the more costly components) may not be essential to eliminate many pathogens from the herd (Table 1, page 8). For example, Clark et al. demonstrated that clinical signs of enzootic pneumonia can be prevented by segregating pigs by age without early weaning or medication. Nonetheless, the swine industry has no irrefutable scientific evidence that vaccinating dams, early weaning, medicating, and age segregation are all required to eliminate certain pathogens. It is not known whether any one of these procedures alone or in different pairs will produce the same results as those reported. The objective of this study was to determine whether various MEW procedures would result in progeny free from the pathogens we identified in the source herd.
Methods

Pigs

Pigs were taken from a 1200-sow commercial herd in which the pathogens listed in Table 1 (page 8) had been identified in diagnostic samples collected in the preceding year. Although *Escherichia coli* diarrhea was a persistent problem, enteric organisms were not considered in this study. Within 24 hours of birth, all pigs were processed as was standard for this herd:

- pigs were injected intramuscularly (IM) with 1 mL (200 mg) of iron dextran and 1 mL of procaine penicillin G;
- tails and canine teeth were clipped; and
- males were castrated.

Housing

Dams all occupied the same gestation room, but were assigned to farrowing rooms by treatment group. After weaning, pigs were housed in L-shaped isolation rooms with floor areas of 9 m². The concrete floors sloped towards corner drains. Water was provided by nipple waterers except for group 4 in which bottle waterers were used to provide water medication. Room temperatures were thermostatically controlled, and rooms were ventilated with positive pressure at 12 air changes per hour. We provided heat lamps for the first 5–7 days in isolation and initial room temperatures were maintained at 34°C. Thereafter, temperatures were reduced by 2°C each week. Pigs were fed on the floor ad libitum throughout the experiment.

Experimental Design

We randomly allocated 60 dams into one of six treatment groups (10 dams per group) at 11 weeks of gestation (Figure 1). From their progeny, we selected a total of 220 gilts and/or barrows that were close to the median weight of each litter to use in the trial. Three pigs from each of the 10 dams in a group were randomly allocated to one of three subgroups:

- one subgroup weaned at 7 ±1 days old;
- one subgroup weaned at 14 ±1 days old; and
- one subgroup weaned at 21 ±1 days old (Figure 1).

Each subgroup was assigned to its own separate isolation room for additional treatment at weaning (Figure 1). Thus, each pig placed in a treatment subgroup represented a litter that could have come from any dam, depending upon the original randomization. In this way, we were able to randomize pigs into both dam and pig treatment groups to statistically test for effect of MEW treatment on the survival of pathogenic organisms.

In addition, we selected 20 barrows from dams in each of groups 1, 4, and 5 (Figure 1), all of which we weaned at 7 days old. These additional 60 barrows remained in their respective isolation rooms until they were 64 days old. The barrows' weights at weaning and at 64 days of age were recorded to indicate any major effect of the treatments on weight gain. However, because of the weakness of randomization procedures for any measures other than organism isolation, this growth data is for observational purposes only.

Treatments

Dams

Dam “full” treatment: We administered the following vaccines at 5 and 3 weeks prefarrowing to sows in treatment groups 1 and 2 (Figure 1):

- rotavirus and transmissible gastroenteritis - modified live virus vaccine (MLV); *E. coli* bacterin-toxoid; *Clostridium perfringens* type C toxoid (ScourShield; SmithKline Beecham);
- parovirus - killed-virus vaccine (KV); pseudorabies virus - MLV; Five Leptospira serovars as bacterins;
### Pig "basic" treatment

- Dams in treatment groups 2, 5, and 6 received no further treatments beyond the routine "basic" treatment vaccinations (described above).

### Pigs

- Pig "full" treatment: Pigs in all subgroups in treatment groups 1 and 3 received the following medications:
  - 200 mg oxytetracycline (LA-200, Pfizer) IM at 1, 5, 8, 11, 15, and 18 days of age, or until they were removed from the farm.
  - 25 mg lincomycin (Lincomix, Upjohn) IM for 3 days prior to weaning (administered by on-farm staff).
  - 300 mg per kg Ivermectin (Ivomec, Merck) with 22.7 mg Enrofloxacin (Baytril, Mobay) at weaning (given subcutaneously by us).
  - Tiamulin (Denagard, Fermenta) at 180 ppm in drinking water for 7 consecutive days after weaning.

- Pig "basic" treatment: Pigs in all subgroups in treatment groups 2, 5, and 6 received no further treatments beyond the routine "basic" treatment vaccinations (described above).

### Other pathogens

- Lung lesions
  - Range of six lesion areas at day tested by pathologist.

### Swine Health and Production - Volume 2, Number 3
standard processing. Group 6 subgroups were not isolated from the source herd.

Pig "basic-plus" treatment: Pigs in all subgroups in treatment group 4 were processed and also received:
- chlortetracycline (Aureomycin® Soluble Powder, Cyanamid) at a dose of 22 mg per kg body weight in their water until they were weaned at 7 days; and
- chlortetracycline and sulfamethazine (Aureomycin® Sulmet® Soluble Powder, Cyanamid) by adding 66 mg of each per L of drinking water for 10 days after weaning.

Feed
All pigs were fed commercial diets throughout the trial. Pigs in subgroups in all treatment groups except treatment group 4 were fed:
- diet A if weaned at 7 days, which contained 165 mg per kg apramycin (Apralan®, Elanco);
- diet B if weaned at 14 days, which contained 55 mg per kg carbadox (Mecadox®, Pfizer);
- diet C if weaned at 21 days, which contained 55 mg per kg carbadox (Mecadox®, Pfizer);
- 3 kg of diet A per pig, 4 kg of diet B per pig, 4 kg of diet C per pig, and then diet D ad libitum in groups 1 and 5 barrows that were not euthanized, until they were sent to the isolated finishing facility. This diet also contained carbadox, but antibiotics were not added to the finishing diets.

Pigs in treatment group 4 did not receive apramycin in diet A; thereafter, they received diets B, C, and D, containing 276 mg per kg chlortetracycline, sulfamethazine, and penicillin (Aureo SP250, Cyanamid), until they were sent to the isolated finishing facility.

**Necropsy and Laboratory Procedures**
Medication procedures were continued for 1 week for each pig subgroup except pig subgroups from treatment group 6. These pigs were weaned, held in isolation for 3 days, and then necropsied.

Three days after we completed the treatments, we euthanatized pigs and performed complete necropsies. We collected serum, nasal swabs, and samples of tonsil, spleen, and lung (1 cm³ of a portion of the ventral part of the middle lobes) from each pig. Isolation procedures were performed on samples from each pig to detect the pathogens listed in Table 1 for the project herd. A fluorescent antibody test (FAT) was used to demonstrate *M. hyopneumoniae* in lungs. Selected lesions were examined microscopically after they were dissected from the lungs, fixed in neutral-buffered 10% formalin, dehydrated in graded alcohols, cut into 6-µm-thick sections, and stained with H and E.

**Retained barrows**
One barrow from each litter of each of these groups (10 barrows per treatment group) was bled at 42 and 64 days of age and tested by indirect FAT for antibody to PRRS virus and for isolation of PRRS virus in porcine alveolar macrophages. On day 64 of the experiment, the 60 barrows were commingled and taken to a clean, empty grow-finish room in an isolated finishing facility, where they were reared for another 90 days.

We took nasal swabs from 16 of the retained barrows for culturing bacteria and then euthanized all barrows. We collected their lungs to estimate the extent of pneumonia. Blood from 26 of the barrows was collected and serum was separated to test for the presence of antibodies to *M. hyopneumoniae* by an ELISA.

**Analysis**
To detect at least one positive sample with 95% confidence in a population of 100 requires:
- five samples when the known prevalence is 50%; or
- 10 samples when the known prevalence is ≥25%. We used the prevalence of pigs from which a pathogen was isolated in the two "basic" groups to determine the prevalence of that pathogen in the randomized population of litters in our study herd. Then, using a sample-size table, we inferred that if we could not isolate a specific pathogen (i.e., *H. parasuis* or *S. suis*) from a group of pigs, the treatment for that group of pigs had inhibited vertical transmission of that pathogen. ANOVA was used to compare differences in weight gain among the three groups of 20 barrows even though the randomization had limitations. Statistical significance was set at *P > 0.05.*

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**Table 1**

<table>
<thead>
<tr>
<th>Infectious Agent</th>
<th>Alexander, et al.</th>
<th>Connor</th>
<th>Wiseman</th>
<th>Project herd*</th>
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*Project herd diagnoses made at the Indiana Animal Disease Diagnostic Laboratory from specimens submitted from the herd of origin used in the project in the year preceding this study.*
Results

During the time pigs were housed in isolation, one pig from group 1 was affected by mild neurological signs and vomited, was treated with penicillin and dexamethasone IM, and recovered within 72 hours. At necropsy, one pig had lesions of exudative epidermitis and four pigs had umbilical abscesses.

S. suis

S. suis was isolated from pigs in all groups at all ages (Figure 1). Serotypes included 2, 5, 6, 7, and 8. Some serotypes reacted with multiple antiseras, and some were untyped. The site most frequently yielding organisms was the tonsils; however, in pigs weaned at 7 days old, S. suis type 2 was isolated from the lungs of one pig in group 2, and untypeable serotypes of S. suis were isolated from nasal swabs from pigs in groups 1 and 3.

H. parasuis

Although hemophilus-like organisms were frequently isolated, some colonies could not be subcultured and we curtailed further attempts to identify them. For pigs weaned at 7 days old, we isolated H. parasuis from groups 2, 4, 5, and 6 (Figure 1). Pigs in group 1, weaned at 14 days, and in group 3, weaned at 21 days, were also free of H. parasuis. The majority of isolates of H. parasuis were from nasal swabs.

Other pathogens

B. bronchiseptica was isolated from a nasal swab of one pig in group 4 weaned at 7 days old. M. hyopneumoniae was identified in the lung of a pig from group 3 weaned at 14 days old, and a non-toxigenic strain of P. multocida type D was isolated from one pig in group 2 weaned at 21 days old. Pseudorabies virus was not isolated from any of the pigs. PRRS virus was isolated from retained barrows in groups 1 and 4, and some barrows in groups 1, 4, and 5 were seropositive to this virus.

Lung lesions

Lesions in lungs of pigs weaned at 7 days old were small and we attributed them to atelectasis. Similar but larger lung lesions in some pigs weaned at 14 days old (from group 5) were confirmed to be areas of atelectasis by microscopic evaluation. Although H. parasuis was isolated from lung lesions of two pigs weaned at 21 days old (group 2), these lesions were also areas of atelectasis.

Retained barrows

Weight gain did not differ (P>05) among the groups of retained barrows. We could not isolate pathogens from the nasal swabs in the barrows that were finished in the isolated facility. Pneumonic lesions occupied ≤2% of the surface area of lungs at slaughter, but none grossly resembled those typical of infection with M. hyopneumoniae. Sera from pigs at slaughter were negative for antibodies to M. hyopneumoniae.

Discussion

In previous attempts to produce pigs free of certain infectious agents:

- dams were vaccinated so that they would develop immunity against endemic pathogens;
- dams and pigs were medicated in an effort to eliminate pathogens; and
- pigs were segregated from dams at young ages to prevent the transmission of pathogens from dams to pigs.\(^{25,6,7}\)

We assumed for the purposes of this investigation that:

- dams were the source of most of the pathogens for pigs;
- antibodies were passed from vaccinated or immune dams to their pigs and this protected pigs from acquiring pathogens during lactation;
- strategic medication of dams and pigs reduced the numbers of pathogens transferred from dams to pigs; and
- early weaning and segregation of pigs further reduced the transmission of pathogens from dams to pigs.

In this study, various organisms were able to colonize the respiratory tracts of pigs weaned at different ages and subjected to various MEW protocols. If an organism survived in one pig of a group, we can assume that all pigs that received similar treatment would be at risk of being infected and developing clinical disease. The prevalence of S. suis and H. parasuis in the pig “basic” treatments was greater than 50% for most groups, thus making it likely that we would have detected these organisms with the experimental design and numbers of pigs we used. However, it is possible that in some groups the prevalence of P. multocida and B. bronchiseptica was too low for us to detect these organisms with our sample size. Nevertheless, under the conditions of our experiment, the rearing conditions may have reduced the likelihood of detecting organisms as much as the medication procedures. Therefore, results of this experiment indicate early weaning and segregation may be the major requirements for deriving pathogen-free and disease-free pigs.

S. suis

S. suis is ubiquitous, can cause serious outbreaks of meningitis, and may be associated with pneumonic lesions.\(^1\) None of the MEW procedures used in this study eliminated S. suis from all pigs in a group. Pigs in group 1 were the most intensely medicated and we anticipated that this group would contain the fewest pigs from which S. suis could be isolated. Isolating even one case of S. suis in a group of pigs meant that MEW procedures had failed to prevent transfer of the pathogen. Thus, the isolation of S. suis in so many pigs in group 1 was inconsequential. If, for example, we had relied on MEW alone for preparing pigs for sale to other herds, there is still a considerable risk that we would have introduced S. suis to naive “minimal disease” or SPF herds.

Clifton-Hadley, et al.\(^{11}\) found that when weaned pigs carrying S. suis were mixed with susceptible pigs, S. suis was isolated from the susceptible pigs within 5 days. However, they had difficulty demonstrating that carrier dams could transmit S. suis to suckling pigs. Thus, Clifton-Hadley, et al.\(^{11}\) concluded that suckling pigs can become infected, but the major spread was probably among older pigs within intensive production units. We were
much more successful in isolating S. suis from weaned pigs in all age groups. We infer that vertical transmission of S. suis is of prime importance. Clifton-Hadley, et al. had success in producing S. suis-free pigs using penicillin in early weaning procedures. Perhaps, therefore, penicillin would have been a more appropriate medication to eliminate S. suis from our early weaned pigs. One pig in group 1 developed neurologic signs at 25 days of age and responded rapidly to medication. Because we did not euthanize the pig to determine if S. suis was involved, we cannot irrefutably argue that MEW prevents the neurologic form of endemic streptococcosis; however, despite many pigs harboring the organism, the virtual absence of neurologic or respiratory disease is encouraging.

**H. parasuis**
The only completely effective treatment for eliminating H. parasuis was a combination of “full” dam treatment and “full” pig treatment. H. parasuis survived in varying proportions of pigs in all other groups (Figure 1). Clinical signs did not develop in pigs from any group including those reared beyond 64 days. As with streptococcus, under commercial conditions H. parasuis has become endemic in naïve and “minimal disease” or SPF herds, and losses associated with disease have occurred. Presumably pigs subjected to MEW, but carrying the organism, would be a potential source of this organism if introduced to a naïve herd.

**A. pleuropneumoniae**
It is possible that the Haemophilus-like organisms that we could not subculture were A. pleuropneumoniae. Generally, in our laboratory, we have little difficulty in culturing, subculturing, or identifying A. pleuropneumoniae and, therefore, we believe it unlikely that the Haemophilus-like organisms we observed were A. pleuropneumoniae.

**B. bronchiseptica and P. multocida**
Single isolates of B. bronchiseptica and P. multocida from nasal passages indicated that both organisms can be transmitted even when pigs are subjected to at least one component of a MEW procedure. Although B. bronchiseptica may cause pneumonia in young pigs, it is of little consequence as a cause of atrophic rhinitis in the absence of concomitant infection with toxigenic P. multocida type A or D. The P. multocida we isolated was a non-toxigenic strain, but a toxigenic strain probably has the same (low) potential to be transmitted as a non-toxigenic strain. Without further evidence from an experiment with a larger sample size, it would be conjecture to argue that the “full” treatment in either dams or pigs alone was completely effective in preventing B. bronchiseptica or P. multocida from colonizing pigs’ nasal passages.

**M. hyopneumoniae**
Although our study design may have limited the likelihood of us detecting M. hyopneumoniae, the lack of seroconversion to this agent in pigs reared to slaughter further supported our contention that all the treatments we used were effective in eliminating this organism from the progeny of the positive dams. Because we found the lesions we examined microscopically to be atelectasis, our concern that M. hyopneumoniae might be transmitted between herds was further reduced. It could be financially significant that we identified M. hyopneumoniae from the lung of one pig that received the “full” pig treatment (which included antimicrobials known to be effective against this organism), because of the possibility of introducing the agent into SPF herds. It is possible ours was a false-positive result, thus strengthening an argument that MEW procedures can effectively reduce the risk of MEW pigs carrying M. hyopneumoniae into a new facility or a herd. Mycoplasmas were not detected in untreated pigs and so it is also possible that the use of isolation facilities alone contributed to eliminating or preventing the spread of this organism.

**PRV**
Procedures adopted for MEW have been shown to prevent the vertical transmission of PRV from seropositive dams to pigs. We also found that PRV was not transmitted from seropositive dams to progeny weaned at 7, 14, and 21 days, thus further supporting the use of early weaning and segregation to produce PRV-free pigs. However, all dams that produced pigs used in this study received PRV vaccine prior to farrowing. Thus, we could not determine whether prenatal PRV vaccines were essential to prevent dams from transmitting the virus to their progeny.

**PRRS virus**
The prevalence of PRRS in the United States has continued to increase since the condition was first diagnosed in 1987 and, in the acute form, has caused severe biological and financial losses in affected herds. Swine industry currently lacks a vaccine to protect pigs against PRRS. Thus, a method of eliminating the disease or, at least, controlling its effects is critical to the industry. Wiseman, in an attempt to prevent severe disease losses in commingled pigs at 10, 15, and 20 days old, used MEW to reduce the risk of vertical transmission of PRRS. Three of the 15 herds from which pigs were selected had been exposed to PRRS virus. Pigs derived from those herds in which PRRS was endemic were raised in isolation facilities with contemporary pigs from other herds and neither group developed the disease nor transferred the virus to pen mates that were derived from apparently naïve herds. Sera from pigs in all three previously infected herds were negative for PRRS virus at the end of the trial. Wiseman concluded that MEW procedures used in their study may have prevented transfer of the virus from dams to pigs or from pigs to pigs.

Dee, et al., in an attempt to eliminate PRRS infection in nursery pigs derived from seropositive dams, used early weaning and age segregation methods. Initially, the nursery pigs remained seronegative. Unfortunately, pigs weaned 3 months after the procedure was instituted were found to be seropositive; however, further segregation techniques in this herd have been successful in producing PRRS-free pigs.

In our study, dams were free of clinical signs of PRRS at the time they farrowed the pigs used in the study, but contemporary pigs in the nursery on the farm of origin continued to develop clinical signs consistent with the respiratory form of
PRRS. Some of our pigs in the groups that were kept until 64 days of age were seropositive at 42 and 64 days of age. Additionally, PRRS virus was isolated from pigs in two of the three groups that we studied. Because we were not able to eliminate PRRS virus, our findings concurred with the initial results of Dee et al.8 Perhaps transfer of the virus from dams to pigs depends upon whether the virus is circulating in the herd at the time that the pigs are weaned. From our results, we concluded that if there was recent clinical evidence of PRRS in the originating herd, early weaning and segregation procedures would not prevent either vertical transmission or horizontal transmission of the virus.

**Weight gain**

From birth to 64 days of age, the three groups of 20 retained barrows (groups 1, 4, and 5 weaned at 7 days of age) gained at the same rate. Thus, we concluded that multiple treatment and handling procedures used in group 1 and 4 pigs were neither harmful nor beneficial to the growth of the pigs when compared to untreated control pigs in group 5.

**Implications**

- We conclude that the early weaning and segregation procedures we used in this study were sufficient to derive pigs with a minimal number of pathogens.
- *H. parasuis* was not transmitted to pigs weaned at 7 and 14 days when both dams and pigs received the “full” treatment. Of group three piglets, only the pigs weaned at 7 days escaped infection; however, there was no evidence of disease in any group of pigs.
- *Actinobacillus pleuropneumoniae* was not isolated from any of our pigs.
- *M. hyopneumoniae* was not detected when any MEW procedure was used.
- Pseudorabies virus was not detected in any pigs used in our study.
- MEW did not prevent clinically normal dams from transmitting PRRS virus to their progeny.
- Vaccinating dams was not beneficial when incorporated in the MEW procedures.
- Neither medications nor vaccinations had an influence on growth performance of the pigs weaned at 7 days and weighed at 64 days of age.

**Acknowledgements**

Financial support was provided by Genetic Improvement Services, American Cyanamid, and Indiana Pork Producers Association.

**References:**

10. Anonymous, Instat™, Graph pad software, San Diego, CA.