Segregated early weaning

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The earliest efforts to use early weaning and segregation technologies to obtain pathogen-free piglets were attempted in the early 1980s.[1] Initially, the strategy called for weaning pigs at 5–10 days of age and relying on medication.[1,2] Later studies suggested that early weaning without medication could also reduce, but not eliminate, the impact of disease in pigs.[3] Since that time, systems using some form of early weaning and segregating pigs from the breeding herd have been rapidly adopted by the United States swine industry.[4] Although several investigators have observed improved growth in pigs undergoing segregated early weaning (SEW),[5,6] these strategies have not proven to be a panacea that eliminates all pathogenic organisms from growing pigs. Often, these technologies are implemented without a full understanding of the underlying physiological principles involved.

Presently, there are five common methods[7] based on the principles of SEW commonly used in the United States swine industry:

- Two-site systems, in which the breeding and farrowing facilities are separated from the nursery and finishing facilities.
- Three-site systems, in which the first site contains the breeding, gestating, and farrowing facilities. Pigs are weaned at 10–21 days of age and moved to a separate nursery (the second site). When the pigs reach 18–23 kg (40–50 lb), they are moved to grower/finisher facilities (the third site). Three-site systems comprise the majority of large scale new construction.
- Commingled three-site systems result when pig flows are not carefully controlled. Pigs arriving at either the nurseries or the finishers are exposed to larger pigs that can't be moved due to delayed rate of gain or large fluctuations in farrowing rate. When pigs are commingled, recently weaned pigs will be exposed to the pathogens of the older pigs.
- Multiple-site systems, in which several sites are used for breeding and farrowing, after which the weaned pigs are transported to a common separate nursery site. Once pigs leave the nursery they are transported to a finishing facility. In this system, there may be several finishing sites. The success of these systems depends on maintaining strict all-in–all-out (AIAO) pig flows so that younger pigs are not exposed to the pathogens of the older pigs.
- Commingled multiple-site systems occur when pigs from different farrowing sites arrive at the same nursery site, providing an opportunity for younger pigs to be exposed to older pigs, resulting in a commingled multiple-site system.

This paper will review the literature regarding some of the more important factors influencing the success of an SEW program—immunology, weaning age, use of medications, growth, and milk antibodies.

Immunology

In SEW, pigs are removed from the sow while their immunity from maternal antibodies is still high (generally ≤ 21 days of age). This strategy assumes that most pathogenic organisms are unable to cross the placenta and that maternally derived passive immunity will prevent vertical transfer of such indigenous pathogens as *Streptococcus hyicus*, *Chlostridium perfringens*, and *Escherichia coli*. Surgical derivation has been used to obtain specific-pathogen-free pigs and gnotobiotic pigs that are free of these bacterial pathogens.[8,9]

It is believed that pigs exposed to antigen will mount an active immune response when passive maternal protection drops below a protective level.[10] Theoretically, early weaning ages also reduce the exposure of pigs to common endemic but nonindigenous pathogens present in their herd of origin.

Investigators have detected the presence of all three classes of immunoglobulin — IgG, IgA, and IgM — in piglet serum after colostrum ingestion. The pattern of decline of these antibodies is nearly exponential, and the half lives of immunoglobulin classes can be determined from the assay of serum concentrations over a period of 2–3 weeks.[11] The rate of decline has been investigated using immunoglobulins labeled with iodine-125, and the mean half lives were determined to be:

- 2.8 days for IgM,
- 2.7 days for IgA, and
- 9.1 days for IgG.[12]

The level of passive immunity in a given population of piglets varies according to the amount of colostrum they ingest.[13] Thus, the ability to mount an active immune response will vary within a population. Management programs that maximize the passive transfer of immunity, such as split-nursing and early cross fostering, should be implemented in SEW systems.

It has been suggested that pathogenic bacteria and viruses produce enterotoxins that induce anorexia;[5] however, various studies have identified other factors that induce anorexia, so the toxins produced by pathogenic bacteria and viruses cannot fully account for why sick animals do not eat normally.[14–18] Klasing has hypothesized that antigen exposure results in the release of cytokines.[19] These cytokines activate the cellular (phagocytic) and humoral (antibody) components of the immune system and serve to further stimulate immunological

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This article is available on the AASP Web site at:
http://www.aasp.org/shap/issues/v5n5/index.html

responses by enhancing the immunological activities of key immune cells (lymphocytes). These cytokines alter various metabolic processes in the body. Voluntary feed intake decreases. Core body temperature and body heat production increase. Overall, body protein synthesis is decreased, and more body proteins are degraded as part of the body's defense to fight the invading pathogens.[19]

Toxins and a variety of pathogenic agents induce leukocytes and other cells of the immune system to synthesize and release the protein molecules we now know as cytokines.[5] Some cytokines, such as interleukin-1 (IL-1) and tumor necrosis factor (TNF), directly and indirectly affect glucose homeostasis, increase net protein oxidation, increase muscle proteolysis, elevate nitrogen excretion, and increase net hepatic anabolism.[20] Cytokines such as TNF cause nutritionally mediated muscle wasting and activate major regulators of metabolic activity — such as the catecholamines — which appear to be essential for the TNF-induced increase in hepatic glucose output.[21] These metabolic adjustments decrease the rate of body growth and result in reduced feed efficiency.[22]

Recent studies have described evidence that some cytokines induce important physiological and behavioral adaptations in sick animals for the purpose of preserving homeostasis. These cytokines alter normal functioning of certain aspects of the neuroendocrine system.[23] Interleukins, which are the products of leukocytes, can act as messengers to inform the brain that a foreign agent has entered the body. These interleukin peptides might form part of a physiological loop between the immune system and the brain.[24]

The brain probably coordinates and activates a variety of physiologic responses—such as anorexia, somnia, fever, and general malaise—in an effort to cope with the invading pathogen.[24] There is evidence to indicate that cytokines that were first isolated from leukocytes are also found in the central nervous system and that they play a critical role in neuropathological symptoms that usually occur in AIDS patients.[25] It is likely that these cytokines are directly responsible for the reduction in feed intake in sick animals, but the actual targets for these cytokines within the CNS are currently unknown.

It is now recognized that leukocytes synthesize and secrete classic growth-promoting molecules, such as growth hormone, prolactin, and insulin-like growth factor I, and all of these molecules affect activities of cells of the immune system.[26] It is likely that cytokines, which are viewed as the major regulators of immune system activity, also regulate other physiologic processes such as food intake in healthy, noninfected animals.[24]

Studies conducted in miniature pigs suggest that swine selected for an enhanced immune response showed favorable growth rates.[27] However, a high prevalence of endemic disease in the herd in which these experiments were conducted may have biased growth rates to favor the high immune responders. This study again demonstrates the herd-specific effects of pathogen control.

Weaning age

Eliminating organisms appears to be more successful at younger weaning ages.[28] Statements like this tend to lead to the conclusion that if young is good, younger is better. Harris[10] suggests the following weaning ages for the following diseases:

Organism	weaning age
Pseudorabies virus	<21 days
Actinobacillus pleuropneumoniae (APP)	<21 days
Mycoplasma hyopneumoniae	<10 days
Pasteurella multocida	<10 days
Haemophilus parasuis (HPS)	<14 days
Porcine reproductive and respiratory syndrome virus (PRRSV)	<10 days
Salmonella cholerasuis	<12 days
Transmissible gastroenteritis virus (TGEV)	<21 days

Pijoan[29] has hypothesized that some diseases may be exacerbated by early weaning ages. He has suggested that maternally derived passive immunity is not high enough to prevent pathogen infection of all pigs in a litter, and that a small proportion of pigs are infected before weaning. Once in the nursery, clinical signs of disease can be observed in a few pigs and large numbers of bacteria are excreted into the environment. Infection spreads slowly during the nursery period, resulting in a larger proportion of pigs expressing clinical disease. This continues until a large proportion of the pigs in the nursery have enough active immunity to prevent clinical disease. The hypothesis is supported by reports that diseases caused by *Streptococcus suis* was increased in early-weaned pigs.[14,15]

Increasing the weaning age results in more pigs being exposed to the bacteria during the lactating period while they still have maternally derived passive immunity. The passive immunity does not prevent infection, but does prevent clinical expression of disease while active immune defenses are being formed.

It is important to develop a herd-specific weaning age dependent upon the pathogen control or elimination objectives.

Use of medications

Several studies have been conducted using SEW techniques in conjunction with antibiotics to eliminate *M. hyopneumoniae* from endemic herds.[14,30] Evidence of *M. hyopneumoniae* infection was not detected in two swine operations over a 12-month period following a low-cost SEW program that involved injecting piglets with oxytetracycline on days 1, 7, and 14 days of age.[30] The piglets were weaned at 14 days of age to offsite nurseries. *Mycoplasma hyopneumoniae* infection was not detected in any of the tests used. Marked improvements in growth rate and mortality were observed in postweaned pigs.

Clark, et al.,[3] noted that the majority of pathogens observed in the breeding herd were not transmitted to pigs that underwent medicated early weaning (MEW) procedures. Isolating pigs was as effective as medication and vaccination protocols in controlling the transmission of pathogens (except for *Haemophilus parasuis*) that were investigated. *Streptococcus* was isolated from pigs in all groups at all ages.

Medicated early weaning did not prevent the transmission of PRRSV from sows to piglets.

In another study of a 140-sow breeding herd with 63% seroprevalence of PRRSV, Dee, et al., attempted to eradicate PRRSV using early weaning and two-site production.[16] Samples taken from pigs raised onsite were positive by indirect-fluorescent antibody (IFA) assay. Ninety samples obtained from pigs offsite were negative for 4 months, but then reinfection occurred. Porcine reproductive and respiratory syndrome virus was isolated from one pig in the nursery and all pigs were seropositive to PRRSV. It is thought that a carrier pig introduced the virus to the herd. Despite the presence of PRRSV infection in the offsite nurseries, there was no evidence of reduced performance or elevated mortality in these pigs.

Thus, there is evidence that, although SEW production in conjunction with medications may be beneficial in some herds, it does not appear to be capable of eliminating all pathogens — *S. suis* and PRRSV were transmitted to early-weaned piglets. Field experience with *S. suis* has shown that depopulation followed by routine cleaning with commercially available disinfectants and a 6-week down time before repopulating was successful in eradicating an unknown type of *S. suis*.[17]

Elevated growth hypothesis

Enlarged thymus weights and an increased thymus:body ratio were found in two studies comparing specific-pathogen-free pigs to conventionally raised pigs.[31,32] The thymus gland is instrumental in the early development of the immune system and its response to foreign antigen. It is believed that infection with pathogens at an early age causes the thymus to decrease in size.

Observations of increased thymus size in SEW pigs compared to conventionally weaned pigs suggests that elevated concentrations of growth hormone and/or growth factors such as insulin-like growth factor (IGF) are responsible for the increased growth rate of SEW pigs.[18]

Effects of orally ingested milk antibodies

Orally administered antibodies from both serum and milk have been shown to protect against enteropathogenic serotypes of *E. coli* in experimentally infected gnotobiotic pigs.[33–35] These studies were conducted on piglets at an age when intestinal absorption of immunoglobulins no longer occurred (> 3-day-old piglets). Wilson[35] determined that the young pig ingested nearly 3 g of immunoglobulin per day. Wilson also determined that a 7-day-old pig could orally ingest as much immunoglobulin each day as it contained in its blood circulation.

Pierce, et al., analyzed three fractions of spray-dried porcine plasma (SDPP) and determined that the beneficial effects from SDPP appear to be associated with the IgG fraction.[36] These findings reinforce the importance of orally ingested immunoglobulins either from the sow or in the feed.

Separation distance and biosecurity

Clark[14] has suggested that the following biosecurity measures be implemented to reduce transmission of pathogens:

- Clean all rooms thoroughly with a high-pressure washer and disinfect with a broad-spectrum product.
- Place rooms so that cross contamination from pigs of other ages is minimized. Avoid common pits.
- If multiple rooms are used so that pigs of many ages are being housed at one site, sequence care of the pigs so that the pigs of highest health status (usually younger pigs) are cared for first.
- Require that workers wear clean clothing and boots to the unit. Workers should be told not to return to rooms with a higher health status after they have been in contact with a lower-health room without proper cleaning and sanitation of clothing and boots.
- Build rodent-proof buildings. If rodents are present, they should be exterminated by a professional exterminator.
- Do not allow vehicles from outside the premises to enter unless they are cleaned and disinfected.
- Place dead animals outside the premises for rendering trucks to remove.
- Load-out facilities should be placed at the perimeter of the premises.
- Visitors should be kept to a minimum and required to wear clean clothing and boots.
- A perimeter fence should be installed around the premises to keep out unwanted visits from people, pets, and feral animals.

Muirhead[37] suggests the following optimal separation distances to prevent airborne transmission of these specific diseases:

- *M. hyopneumoniae*: 2 miles
- pseudorabies virus: 5 miles (PRV transmission has been documented to spread 50 miles over water)
- *Streptococcus suis*: 2 miles
- TGEV: 300 yards (TGEV transmission has been documented to spread several miles via birds)
- *A. pleuropneumoniae*: 300 yards
- *Serpulina hyodysenteriae*: 300 yards
- *Pasteurella multocida*: 300 yards

Discussion

The complex interplay of management and disease suggests that health management decisions should be made as part of an overall evaluation of the herd, instead of focusing on individual pathogens.

If the main objective of SEW is to separate pigs from the pathogens associated with the sow herd and to avoid the exposure of recently weaned pigs to the endemic nonindigenous pathogens of older pigs, then a knowledge of the specific pathogen load that is affecting each herd is required. It is possible that in some single-site herds, where strict attention has been paid to biosecurity and pathogen prevention, very little advantage may be observed in moving pigs off-site.[38]

Implications

- Complex pork production practices create an opportunity to apply veterinary techniques, including epidemiology and diagnostic procedures.
- A complete understanding of immunologic principles and pig management practices will aid in determining when the pathogen prevention practices fail in a production unit.
- The health status of the sow herd should be determined before implementing pathogen control strategies that include site separation.
- Pathogen control strategies that include SEW will need to be production-system specific, and biosecurity measures strictly enforced.
- Veterinarians will be challenged to determine whether site segregation practices are actually preventing the horizontal transmission of pathogens.

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