COSTS, CONSEQUENCES AND CONTROL OF ENDEMIC DISEASES

Gary Dial[*], Chris Rademacher[*], Barry Wiseman[+], Janelle Roker[*], and Bradley Freking[*]
[*]New Fashion Pork, Inc., Jackson, Minnesota
[+]Nextran, Inc., Princeton, New Jersey

INTRODUCTION

Now more so than ever, pig production is a competitive business. Producers are being forced to cut costs, just so that they can survive the competitive challenges proffered by other pork producers and other producers of meat protein. The optimization of revenues has become a dire necessity to those who want to continue making their living raising pigs. We have entered a stage in the competitive evolution of the pork industry when we are being forced to consider any technology promising an advantage either in terms of cost management or revenue enhancement. Fortunately, the developed world has put in place, over the last couple of decades, genetic programs in swine that are making us competitive with other producers of meat protein. These genetic advances have enabled us to take advantage of recent, highly promising scientific developments in nutrition and health. Consequently, most of us have begun to learn how to feed pigs and how to manage health influences on nutrient utilization. The intent of this paper is to highlight, in practical terms, contemporary knowledge on the costs and consequences of endemic diseases of pigs. A special emphasis will be placed on how diseases affect the growing pig. At the risk of adulterating good science with empirical observation, we will also describe the practical approaches that we use to control endemic diseases in our production system.

AN EMERGING MODEL FOR HOW DISEASE AFFECTS THE HOST

The epidemic manifestations (i.e. acute effects) of infectious agents are better understood than endemic effects. For example, we generally understand how Porcine Reproductive and Respiratory Syndrome (PRRS) virus affects fertility, abortion rates, and pre- and post natal survival. Similarly, most of us also have long understood that exposure of naïve growing pigs to *Mycoplasma hyopneumonia* (MHP) results in reduced growth performance, more variable growth rates, and higher mortality rates. What we have not understood well, at least until recently, is how endemic diseases affect the pig. Recent research has demonstrated that endemic diseases detrimentally influence pig performance without causing overt clinical signs. We have learned that infectious agents not only induce an immune response designed to clear the agent from the body but that the immune system induces cascading effects, many of them detrimental to growth, on the host's metabolic processes. Based upon replicated experiments conducted in several species, including the pig, a hypothesis is emerging which ties together the myriad of independent observations uncovered by contemporary science. This hypothesis links the health and immune function of the pig integrally with its nutrition through hormonal messenger systems. While it is still a hypothesis, the growing consensus of scientists working in the area is that technologies which minimize the activation of the pig's immune system will enhance the rate and efficiency of body weight growth while improving the deposition of carcass lean throughout the pig's life.

Several types of studies have been conducted in the pig investigating the effect of diseases on metabolism and immune function; they generally show highly similar results. Some studies have compared the metabolic and immune changes in segregated, early weaned (SEW) pigs versus pigs reared in traditional environments (Williams et al., 1997a,b,c). Others have contrasted the response of pigs exposed to specific pathogens with those of non-exposed pigs. Disease processes examined, thus far, include a variety of agents that currently challenge the modern swine industry, including: PRRS (Greiner et al., 2000), MHP (Escobar et al., 2002), *Actinobacillus pleuropneumonia* (APP) (Balaji et al., 2002), and *Salmonella typhimurium* (STM) (Balaji et al., 2000). Using an experimental model commonly used to study disease processes in other species, other investigators have contrasted the responses of pigs to lipopolysaccharide (LPS) extracts from the cell walls of E. coli to those of non-exposed pigs (Sauber et al., 1999; Wright et al., 2000). Collectively these studies demonstrate that during periods of health challenge, immune substances orchestrate a metabolic response to the infection such that nutrients are directed away from tissue growth in support of immune function. Even when serial disease challenges are subclinical in nature, there is a cumulative effect sufficient to cause significant alterations in metabolism with concurrent losses in performance.

METABOLIC EFFECTS OF DISEASE

Exposure of an animal to pathogenic (e.g. viruses, bacteria) or nonpathogenic substances (e.g. endotoxins present in the pig's environment) results in the release of immune substances from the inflammatory cells (e.g. macrophages) present in the blood and tissues (Klasing, 1988). These substances activate the immune system, reducing appetite and altering metabolic processes. The metabolic changes may include an elevation of the basal metabolic rate and a shift in how both ingested and stored nutrients are used by the body. There may or may not be a slight, transient elevation of body temperature in response to the body's release of inflammatory mediators combating the foreign invader. Not uncommonly, no outward manifestations of the endemic disease process are observed.

The body's hormonal system appears to be a key to the shift in metabolic processes. While it is less clear in the pig, the secretion of anabolic hormones, such as growth hormone (GH), is reduced in other mammalian species (Spurlock, 1997). Anabolic hormones stimulate the deposition of nutrients in tissues, and the development and proliferation of cells. Being dependent upon GH secretion, the release of other anabolic hormones, such as insulin-like growth factor (IGF) from the liver, is diminished following immune challenge. While the secretion of anabolic hormones is compromised, the release of catabolic hormones is stimulated. Catabolic hormones stimulate tissue breakdown and the mobilization of body stores of nutrients. Glucocorticoid hormones are released from the adrenal glands in response to the central actions of inflammatory substances on the brain. These prevent the deposition of nutrients, such as glucose and amino acids, in muscle, mobilizing them for use by the immune machinery as it fights off infections.

Collectively, the immune-mediated effects on the hormonal system induce a shift in the way nutrients in the body are transported and utilized. In animals challenged by infectious agents, glucose uptake by tissues is dampened as the body seeks to repartition energy to meet the energetic demands of the immune system. Products of the body's immune response to infection induce a resistance by the body's peripheral tissues to insulin, the hormone involved in glucose regulation. Consequently, glucose uptake by skeletal muscle and adipose tissue as well as key internal organs, such as the heart and liver, is compromised. Insulin, which functions in part to lower circulating levels of sugar by driving tissue uptake, is less able to preserve liver and muscle stores of glucose during periods of immune-system activation.

Protein and amino acid metabolism is also modified under immune challenge. During endemic infections, the liver augments its stores of amino acids so as to enable the body to meet its increased requirement for the amino acids incorporated into substances produced to combat infections. Blood flow to the liver as well as amino acid transport into cells is augmented during times of infection. The modification of liver function appears to be the consequence of the effects of the glucocorticoids on receptors in liver cells producing immune mediators (i.e. cytokines). In contrast to the liver, skeletal muscle uptake of amino acids is suppressed during periods of immunological stress.

In sum, it appears the peripheral tissues, such as skeletal muscle and adipose, are deprived of nutrients as a consequence of the orchestrated effects of immune substances on insulin responsiveness and glucocorticoid secretion. The net result is that immune responses precipitate a flux of amino acids from skeletal muscle pools to the liver. If the immune response is prolonged, skeletal muscle pools may be depleted of essential amino acids.

PHYSIOLOGICAL EFFECTS OF DISEASE

Protein. The accretion of protein in skeletal muscle reflects the balance between relative rates of protein synthesis and degradation. When animals are challenged by disease, protein synthesis is lowered while protein degradation is accelerated. As described in detail by Spurlock (1997), the balance between synthesis and degradation shifts toward degradation as a consequence of at least three things, two of which have been previously discussed. First, the release of immune substances following exposure to disease agents is often associated with reduced feed intake; thus, the body's supplies of amino acids are progressively consumed as the body's defenses wage an ongoing war against invading pathogens. Second, the immune responses mounted by the host to confront a infectious agent requires the consumption of amino acids in the synthesis of acute phase proteins from the liver and other products of immune tissue (e.g. antibodies). Lastly, because of the mismatch in the amino acid composition of muscle and immune products, the body is forced to catabolize a disproportionate amount of muscle in order to achieve the necessary complement of amino acids needed by the immune system. Thus, protein losses during an immunological challenge are greater than what can be sustained by feed intake, especially if it is reduced.

Skeletal muscle may not be the only source of protein used by the body during periods of infection. In other species beside the pig, the intestinal tract has been found to be a source of

amino acids required by immune synthetic processes. The body apparently is able to activate multiple proteolytic processes as it robs nutrients from tissues having a lower priority, making them available for the immune systems. It appears that the body will readily consume itself as it prioritizes resources for its fight with invasive challenges.

Fat. In addition to effects on protein synthesis, the catabolic processes initiated by immune-challenged pigs also encompass major shifts in fat metabolism. Typically, as energy is consumed during periods of immune activation, fat reserves are broken down as a source of energy. Immune substances secreted as the body fights off infections induce the expression of genes involved in the production of lipase enzymes. These enzymes cleave lipoproteins to triglycerides and then to free fatty acids and glycerol, which are used as energy by the immune system.

CONSEQUENCES OF DISEASE

Growth Performance. As mentioned, immune modulators cause reductions in appetite, divert nutrients from muscle to the immune system, and depress protein synthesis while stimulating protein degradation by skeletal muscle. Consequently, pigs endemically infected with disease agents experience reductions in average daily feed intake (ADFI), average daily body-weight gain (ADG), and the efficiency of conversion of feed to body weight gain (FCE). Differences between challenged and unchallenged pigs persist throughout the growth phase, from weaning to market (Williams et al., 1997 b,c). This prolonged effect of the immune system persists even though one would expect the pig to be less immunologically susceptible to pathogen challenge during the late growth phase. Poorer ADG and FCE are due, in part, to reduced ADFI. However, immune-mediated perturbations in anabolic and catabolic hormone release and associated metabolic shifts in muscle protein retention are thought to be the principle causes of reduced growth performance.

The amount of dietary lysine required to maximize ADG and FCE is greater for pigs that are not immune challenged versus those that are undergoing endemic infections (Williams et al., 1997 a,b). The reduction in lysine use by challenged pigs appears to be attributable, to a modest extent, to poorer digestibility (perhaps as a result of immune-mediated intestinal wall damage) and, to a greater extent, to a compromised ability to deposit protein. The higher protein accretion occurring in non-challenged pigs is associated with a higher demand for energy, particularly during stages of growth when energy intake is limiting. Health challenged pigs have a lower efficiency of energy utilization in association with the overfeeding of protein. Apparently, energy is consumed in challenged pigs in the elimination of excess protein. While nutrient needs for growth differ dramatically, maintenance requirements are similar for challenged and unchallenged pigs.

Carcass Characteristics. The carcasses of pigs that are health challenged have a lower protein:lipid content than those of non-challenged pigs (Williams et al., 1997 b,c). Pigs that are not exposed to pathogens accrue both protein and lipid at a faster rate than diseased pigs; however, the rate of fat accretion as a proportion of body weight is lower in unchallenged than challenged pigs. Carcasses from non-challenged pigs have less backfat, larger longissimus

muscle areas, and greater overall carcass muscle content than diseased pigs. In addition, pigs that have not undergone immune stimulation had lighter liver, heart, lungs and gastrointestinal tract weights and less leaf fat than immune-challenged pigs. In sum, these observations indicate that pigs that remain healthy throughout their growth period will have higher yields and a greater percentage of lean and primal cuts.

Pregnancy. Numerous studies have demonstrated that some pathogens have an affinity for the various tissues of the developing embryo or fetus. The consequences of such infections include: increased rates of abortion and pregnancy termination (resulting in lower farrowing rates), increased embryonic and fetal mortality (resulting in smaller born-alive litter sizes), and increased peri- and post natal mortality (resulting in smaller weaned litter sizes). In addition to these affects, the results of several recent studies, as reviewed by Spurlock (1997), suggest that immune challenge of the pregnant female also has more subtle affects on the developing fetus that include alterations in the metabolic processes of the placenta.

The fetal immune system becomes potent to respond to agents that cross the placenta as pregnancy advances. In a manner similar to the postnatal pig, fetal growth and development apparently is altered by challenges occurring during gestation. When exposed to foreign substances crossing the placenta, the immune system of the fetal pig precipitates metabolic changes, similar to the post natal pig, which divert nutrients from growth to the production of immune products. In addition, placental transfer of amino acids is compromised during periods when the sow is immune challenged, resulting in reduced nutrient availability to the developing fetus. The combined consequence of fetal immune system activation and maternal immune effects on the placenta is that the growth and development of the fetus is retarded, especially if the health challenge occurs during a critical phase of development. The result is lower birth weights, more variable birth weights, a higher proportion of low-viability pigs and fetal abnormalities.

Prenatal exposure to pathogens also appears to affect the proliferation and differentiation of tissue precursor cells (Spurlock, 1997). Substances associated with the immune response act synergistically to retard the differentiation of precursor cells for both muscle (myoblasts) and fat (adipocytes). The potential, therefore, exists for prenatal immune challenges to cause permanent alterations that are carried over postnatally to production and carcass traits.

Lactation. The exposure of lactating sows to lipopolysaccharide (LPS) has long been known to disrupt the secretion of hormones required for the maintenance of lactation (e.g. prolactin, GH, IGF). Sows exposed to LPS during lactation have depressed appetites, lower daily milk production and lighter litter weight gains. Total milk protein and milk energy are reduced in LPS-challenged sows, even though milk composition is not changed (Sauber et al., 1999). Apparently, immune-system challenge interferes with the mammary gland's ability to produce milk, when the amount of nutrients derived from the diet and mobilized from tissue reserves cannot match the needs of the body for both its immune response and milk production.

ENDEMIC DISEASES CHALLENGING THE SWINE INDUSTRY

All pathogens that cause an immune response in the host have the potential to disrupt metabolic processes, thereby interfering with nutrient utilization. The body mounts immune responses whenever any organ system is infected, whether the infection resides in the respiratory tree, the gastrointestinal or urogenital tracts, joints, or CNS. Blood-borne infections as well as localized infections of organs perturb the body's metabolism through effects on the immune system. In recent years, endemic diseases such as APP, swine dysentery, pseudorabies, mange, and lice have been largely eliminated from the herds of progressive producers. We call these Type 1 infections and believe that there is no excuse for producers tolerating infections of this type. Presently, approaches for the elimination of endemic infections with agents such as PRRS and MHP are being investigated. We call these Type 2 infections and believe that producers are currently under considerable pressure, for economic reasons, to eliminate endemic infections of their herds with these agents. In the future, it is likely that diseases such as *Salmonella cholerasuis* (SCS), ileitis, swine influenza virus (SIV), *Hemophilus parasuis* (HPS), *Actinobacillus suis* (AS), and *Streptococcus suis* (SS) will be targeted for elimination. These are Type 3 diseases. While we believe that endemic infections of these agents are economically important to the producer, they will be more difficult to eliminate from and/or keep out of a herd. Ultimately, we believe that swine producers will be forced by market forces and, perhaps, legal pressures to eliminate agents that are pathogens to humans but relatively inconsequential to the pig. We call these Type 4 diseases.

We speculate that as each of the Types 1, 2 and 3 diseases is sequentially eliminated, there will be a step-wise improvement in growth performance and, conceivably, increases in carcass value. As preventative and therapeutic treatments are reduced, facilities are used more efficiently, and productivity improves, costs of production will decline synchronous with the elimination of each endemic disease.

DISEASE CONTROL STRATEGIES

More because of the effects of endemic than epidemic diseases, the swine industry is likely to develop a growing intolerance of diseases. Historically, we have focused on diseases that cause mortality in growing pigs or infertility in the sow herd. In the future we will be increasingly concerned about diseases that chronically affect the growth performance of our pigs, reduce carcass value, and keep us from consistently weaning a high quality pig that does not carry infections with them into the growing phase. Approaches for managing endemic diseases will have near-term and long-term components.

Near-term Strategies. The near-term disease-control objectives for most producers are to (1) wean naïve pigs from sow herds that are endemically infected with either Type 1 or 2 pathogens and (2) keep them from becoming infected during the growing phase.

We believe that the health status of the growing pig herd is integrally related to the status of the breeding herd. Sow herds that have circulating PRRS, MHP or other agents will likely

pass on those agents to their offspring prior to weaning. Current strategies for reducing the occurrence of immune challenges of the growing pig herd include several technologies designed to first stabilize, then slowly upgrade the health of the commercial breeding herd.

- Populate gilt multipliers, genetic nucleus farms and boar studs with breeding stock that are free of Type 1 and Type 2 diseases.
- Wean naïve gilts into dedicated gilt development units, which are used to ensure that incoming gilts are immune to endemic diseases and non-shedding before they enter the commercial herd.
- Minimize litter-to-litter transfers of suckling pigs, so that moved pigs do not transfer infectious agents from an infected sow to the pigs from another litter.
- Establish separate breeding, gestation, and farrowing flows for gilts and sows within each breeding herd, so that gilts and sows are housed separately.
- Segregate pigs weaned from gilts from those coming from sows.
- Wean pigs a minimum of 16 days, so that they start well during the nursery phase; avoid weaning pigs more than 7 days older than the youngest pigs weaned in the group.
- Avoid co-mingling of pigs from multiple sow farms.

Once weaned, there are several production systems being used to keep the pig free of infection.

- Rear pigs all-in/all-out by barn and by site, as possible.
- Restrict the number of finishing barns on a site to what can be filled within 1 week.
- Use wean-to-finish technologies in place of conventional 3-site production.
- Place pigs in geographic pods of barns containing only pigs from the same sow farm source.
- Use vaccines when there are effective commercial or autogenous vaccines, and when it is likely that pigs will be exposed to an economically challenging agent (e.g. ileitis, salmonella, MHP, SIV).

Long-term Strategies. The long-term health objectives of producers will likely be to: (1) wean pigs from sow herds that are endemically infected with Type 3 pathogens, (2) control non-specific challenges to the immune system, and (3) eliminate the risk of consumers being exposed to contaminants in pork (i.e. food-borne pathogens of humans, antibiotics).

Production systems that we expect to be put broadly in place in the future include:

- Populate all commercial sow farms with high health breeding stock free of Type 1, 2 and 3 diseases.
- Populate all herds with breeding stock that is free of Type 4 agents having zoonotic potential to human consumers.
- Rear pigs in geographic areas where there is reduced likelihood of cross-contamination from nearby herds.
- Eliminate the use of feed-grade and non-therapeutic antibiotics and growth promotants.
- Increasingly broad use of specific vaccines to prevent pigs from becoming infected.

LITERATURE CITED

Balaji, R., Wright, K.J., Hill, C.M., Dritz, S.S., Knoppel, E.L., and Minton, J.E. 2000. Acute phase responses of pigs challenged orally with *Salmonella typhimurium*. J. Anim. Sci. 78:1885-1891.

Balaji, R., Wright, K.J., Turner, J.L., Hill, C.M., Dritz, S.S., Fenwick, B., Carroll, J.A., Zannelli, M.E., Beausang, L.A., and Minton, J.E. 2002. Circulating cortisol, tumor necrosis factor-alpha, interleukin-1 beta, and interferon-gamma in pigs infected with *Actinobacillus pleuropneumonia*. J. Anim. Sci. 8:202-207.

Escobar, J., Van Alstine, W.G., Baker, D.H., and Johnson, R.W. 2002. Growth performance and whole-body composition of pigs experimentally infected with *Mycoplasma hyopneumoniae*. J. Anim. Sci. 80:384-391.

Greiner, L.L., Stahly, T.S., and Stabel, T.J. 2000. Quantitative relationship of systemic virus concentration on growth and immune response in pigs. J. Anim. Sci. 78:2690-2695.

Klasing, K.C. 1988. Nutritional aspects of leukocyte cytokines. J. Nutr. 124: 906-1003.

Sauber, T.E., Stahly, T.S., and Nonnecke, B.J. 1999. Effect of level of chronic immune system activation on the lactational performance of sows. J. Anim. Sci. 77:1985-1993.

Spurlock, M.E. 1997. Regulation of metabolism and growth during immune challenge: An overview of cytokine function. J. Anim. Sci. 75:1773-1783.

Williams, N.H., Stahly, T.S., and Zimmerman, D.R. 1997a. Effects of chronic immune system activation on the rate, efficiency and composition of growth and lysine needs of pigs from 6 to 27 kg. J. Anim. Sci. 75:2463-2471.

Williams, N.H., Stahly, T.S., and Zimmerman, D.R. 1997b. Effects of chronic immune system activation on body nitrogen retention, partial efficiency of lysine utilization and lysine needs of pigs. J. Anim. Sci. 75:2472-2480.

Williams, N.H., Stahly, T.S., and Zimmerman, D.R. 1997c. Effects of level of chronic immune system activation on the growth and dietary lysine needs of pigs fed from 6 to 112 kg. J. Anim. Sci. 75:2481-2496.

Wright, K.J., Balaji, R., Hill, C.M., Dritz, S.S., Knoppel, E.L., and Minton, J.E. 2000. Integrated adrenal, somatotropic, and immune responses of growing pigs to treatment with lipopolysaccharide. J. Anim. Sci. 78:1892-1899.