

Arthritis or OCD - Identification and Prevention

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■ Introduction

Structural lameness in swine has persisted despite decades of improvements in genetic, nutrition, disease, and housing management practices. Osteochondrosis (OC) is the most prevalent cause of structural lameness in growing swine. Osteochondrosis can progress to osteochondrosis dissecans (OCD) and osteoarthritis (OA). Even after decades of research, the specific failures in cellular mechanisms that initially trigger these disorders are unknown. Much progress has been made to describe tissue and cellular alterations that occur with each syndrome, but principle signals remain elusive. Thus, the disorders would be correctly identified as idiopathic, ie., a disease of unknown cause or origin. Before discussing the management techniques recommended to reduce losses associated with OC, OCD, and OA, a brief definition and description of each disorder will be provided with an overview of recent research progress that offers insights into potential causes of the disorders.

Insightful and extensive reviews have been published on these disorders in swine and humans. Recommended reviews include Nakano et al., 1987; Hill 1990; Merck, 1991; and Sarzi-Puttini, 2005.

■ Definitions

Definitions of OC, OCD, and OA were adopted from more detailed descriptions provided by Siffert, 1981; Palmer, 1985; Hill, 1990; and Merck, 1991.

Osteochondrosis

Osteochondrosis (OC) is identified as a non-infectious disturbance of endochondral ossification i.e., the process of bone accretion at growth plates via formation of a cartilage matrix. Lesions occur at either the epiphyseal growth plate and/or the articular-epiphyseal cartilage complex just beneath the joint surface cartilage. Initially, these lesions involve a focal thickening of cartilage, but may progress to streaks in the articular cartilage and/or focal regions of retained cartilage in the subchondral bone. Both cartilage and subchondral bone are involved in final lesions. The lesions are associated with either necrotic chondrocytes or poorly mineralized chondrocytes in the articular-epiphyseal cartilage complex that fail to be reabsorbed and replaced with bone. Continued progression of OC disorders may eventually lead to OCD or OA. Humans and animals, particularly swine, horses, poultry, and certain dog breeds, are affected by OC lesions. Lesions are more evident during periods of rapid growth.

Osteochondrosis dissecans

A progression of OC to a debilitating disorder, known as osteochondrosis dissecans (OCD), is characterized by dislodged segments of epiphyseal and/or articular cartilage resulting in exposure of mineralized subchondral bone. In some cases the cartilage may re-attach and heal to form a wrinkled articular surface.

Osteoarthritis

Osteoarthritis (OA) also involves a progression of OC to an irreversible debilitating condition. In OA the articular cartilage also becomes eroded with exposure of the subchondral bone as in conditions of OCD. The major difference between OCD and OA involve mineralization of tissues surrounding the joint and excessive mineralization of bone. The synovial membranes become calcified and surrounding tissues are invaded by calcified outgrowths (osteophytes). In OA bone the joint surfaces become hardened (sclerosis). The joint space is often reduced and bone surfaces become distorted.

Inflammatory arthritis

In contrast to OA, inflammatory arthritis (IA) produces proliferation of joint tissue with a thickening of the joint capsule and an increased accumulation of synovial fluids that may contain blood or fibrin. Common pathogens in pigs that may cause inflammatory arthritis include erysipelas, streptococcus, haemophilus, and mycoplasma organisms.

Osteoporosis

Osteoporosis (OP), another common bone disorder, involves a loss or thinning of mineralized bone tissue. Osteoporosis is prevalent in elderly human populations, but can cause lameness in swine, particularly in breeding animals. The lack of mineralized bone tissue results in bone fractures and contributes to a major cause of culling in the breeding herd.

The focus of this paper is OC, OCD, and OA. Descriptions of IA and OP are offered to distinguish different disorders that also contribute to swine lameness. The latter disorders (IA & OP) and disorders of the hoof and footpads will not be specifically addressed, but certainly contribute to the overall symptoms of lameness in swine.

■ **Historical Perspectives of OC and OA in Swine**

In a 1987 comprehensive review of leg weakness and OC in swine (Nakano et al., 1987), the authors at one point stated, "Thus, osteochondrosis has been thought to be an important predisposing factor to leg weakness in swine and its etiology has been a major concern among researchers for the past 15 years". Unfortunately the statement is still true today, almost 20 years later. After almost 35 years of effort the etiology of OC in pigs is still unknown. Over the same period efforts to understand similar conditions in dogs, horses, poultry, and humans have occurred but, as in swine, the efforts have not provided a clear etiology of OC disorders. However, great strides have been made in understanding cellular events of bone and cartilage growth and key signals involved. With a better understanding of the cellular signals involved in bone and connective tissue growth, perhaps treatments to intervene and ultimately cure OC disorders can be found.

Lesions associated with OC are not the results of "modern" swine management procedures. Hill (1990) noted that OC has existed in swine for at least 60 years. Reports cited (Hill, 1990) from 1925 described lesions consistent with OCD, but differences in terminology and histological descriptions made comparisons with more recent reports difficult. The incidence of the initial stages of OC lesions (not equivalent to incidence of clinical lameness) in swine were estimated at 80 to 100% in the 1960's and 1970's. Estimates today are slightly lower, but approximately 80% of pigs marketed today are thought to have slight to mild forms of OC lesions. Given the extensive historical occurrence of OC in swine over a period in which dramatic changes have occurred in management, can we conclude that changes in management techniques such as genetic selection, nutrition, housing and etc., have not exacerbated nor prevented the lesions?

■ Factors that contribute to OC, OCD and OA

Within traditional disciplinary boundaries, swine researchers have explored genetic, nutritional, disease, and housing factors thought to impact incidence and progression of OC disorders. New techniques now allow insights into cell signals involved in the intricate control of endochondral ossification (bone formation from cartilage). These techniques bridge across traditional boundaries and allow researchers to quantify and identify numerous signals in cells that determine if cells, and ultimately the entire tissue, functions properly. Aberrations in any of these signals or cell growth factors may cause miscues that trigger focal failures in cartilage growth. Orth (1999) identified at least nine growth factors critical in the initial stages of endochondral ossification. More recently Pelletier and Martel-Pelliter, (2002) focused on the matrix metalloprotease family of proteins, specifically collagenase-3, as a pivotal group of proteins involved in degradation of OA cartilage. Drugs that specifically block collagenase-3 are now used for OA treatment in humans. Attempts to intervene at earlier stages of OC disorders by targeting initial cellular events involved in formation of OC lesions offers promise.

Identifying which signals or events to target offers a challenge. Numerous cell signals are involved. Compounds such as insulin-like growth factor (IGF-1) and the IGF-1 binding proteins affect cartilage formation in localized regions. The production of IGF-1 binding proteins are influenced by prostaglandins, specifically PGE². The pro-inflammatory cytokine, interleukin-1B (IL-1B) is also thought to be an initial trigger involved in cartilage degradation. Excess production of nitric oxide (another class of cell signals) was observed in cartilage cells from OC lesions. Inhibition of nitric oxide production reduced the progression of OA in an animal model. Within 2 days of an OA induced lesion, proteoglycan synthesis was inhibited. The presence of IL-1B and the protein required for nitric oxide synthesis was evident before other cytokines or cell signals were detected (Dumond et al., 2004). Thus, IL-1B and nitric oxide production appear to be early targets that could be disrupted to limit formation of OC lesions.

Normal cartilage development involves a loss of vascular supply with age and the cartilage layers become thinner. Disruption of this process may result in development of OC lesions (Ytrehus et al., 2004). Physical disruption of the vascular supply induces histological lesions consistent with OC in rabbits (Kajiwara et al., 2005) and pigs (Carlson et al., 1991). The cellular signals that fail to respond, or that over respond and allow disruptions of vascular supply are not known.

Disruption of the vascular supply induces histological lesions consistent with Osteochondrosis

The role of subchondral bone in OA development continues to provide interesting links and may be involved in the onset, rather than just a consequence, of cartilage problems. Aberrant signals from subchondral bone cells may result in a disruption of the normal process of vascular invasion and replacement of cartilage with bone. Likewise, subchondral bone properties may affect distribution of loads and create focal failures in cartilage. Subchondral bone from humans with OA was three times stiffer and stronger than bone from control patients (Sinigaglia et al., 2004). While excess cartilage compressive stiffness is one of the early symptoms of OA (Felson et al., 2000), cartilage erosion did not appear until the compressive stiffness was lost. The potential for early effects of subchondral bone involvement in OA has been recently reviewed (Burr, 2004). Increased density of subchondral bone altered bone stiffness and increased stresses imposed on cartilage. Whether excessive levels of dietary Ca and P can also alter subchondral plate density and stiffness is not known, but Ca and P are directly involved in the maturation and differentiation of cartilage cells (Wang et al., 2001).

Genetic

Natural selection pressures should eliminate or reduce the severity of OC disorders as lameness associated with OC is often exhibited by puberty. However, associations among production traits and genes associated with OC disorders have apparently precluded natural selection processes from elimination of the disorder.

Heredity

The search for a genetic basis for OC and related disorders is hampered by the complexity of changes that can induce aberrant tissue. A single point mutation in a structural protein, or even a protein involved in synthesis of a cell signal or receptor can induce a cascade of events leading to a lesion. In a review of the genetic basis of OA, Holderbaum et al. (1999) concluded that a single gene mutation was unlikely to explain all the interactions of protein mutations that could result in OA disorders. More likely polygenic mutations with considerable interactions of environmental factors are explanations for OA phenotypes.

Genetic pre-deposition to OC, OCD and OA: selection for growth and production traits

Genetic and phenotypic correlations between OC and production traits were recently reported (Kadarmideen et al., 2004). Unfavorable associations among production traits (growth, feed efficiency, meat quality traits) and OC lesions were detected, implying that selection for production traits will inadvertently result in selection for OC lesions.

Environmental Factors

The understanding of OC disorders must incorporate the molecular basis of gene expression in the initiation and progression of OC. Environmental factors thought to be important in modulation of gene expression include nutrition, disease, and physical weight-bearing conditions.

Nutrition

In their review of OC in swine Nakano et al., 1987 discussed the potential role of various nutrients to alter the incidence and severity of OC lesions. The authors concluded,

“At present, there is no evidence to support a therapeutic or preventative effect of increased nutrient intake on locomotory problems of swine and although many nutrients have not yet been studied in this context, it does not appear to be a rewarding avenue of investigation.” The nutrients reviewed included Ca, P, vitamin C, biotin, Cu, and vitamin E. Questions about the potential for an effect of maternal nutrition on the incidence of OC in offspring and effects of dietary acidosis were identified but not discussed in detail. In addition to nutrients discussed by Nakano et al., dietary interventions that potentially affect OC lesions include dietary fatty acid sources (n-3 vs n-6 fatty acids) and glucosamine. These interventions are discussed below.

Disease

No evidence exists to support that the induction of OC disorders is primarily a result of responses to pathogenic organism(s). However, secondary consequences of certain diseases will exacerbate pre-existing conditions. These secondary consequences may be as simple as traumatic injuries often experienced by animals weakened from disease, or as complex as alterations in cytokine signals which stimulate aberrant responses in cartilage and bone tissues. The impacts of intensive vaccination protocols on modification of cellular signals in bone and cartilage tissues are not known.

Housing

While load-bearing and trauma affect the incidence and extent of OC lesions, evidence to support or reject a specific housing type is not available. The historical occurrence of OC across numerous changes in housing conditions preclude housing as a primary cause. Certainly trauma associated with slippery conditions on frozen dirt lots or wet concrete surfaces can exacerbate OC lesions and increase likelihood of OCD or OA lesions in pigs.

In a recent survey of the reasons for culling sows from 10 Danish herds (Kirk et al., 2005) housing conditions included tethered systems and group penning systems with the use of bedding. No distinctions among housing types were

evident. Locomotive disorders accounted for 72% of culled sows. Most of the lame sows (24%) were culled for OA. Bone fractures were the second major reason sows were culled, accounting for 16% of the culled sows.

■ Management Recommendations - What Can Be Done

The following comments reflect the author's opinions on common management issues often linked with OC disorders. Good management practices may often alleviate some of the pain associated with extreme progression of OC lesions. However, dramatic modifications in sound management practices, nor promotions of an alternate management procedure to prevent or eliminate OC are not supported.

Genetic Seedstock Selection

Genetic predisposition to OC is evident, as discussed above, but the lack of definitive diagnostic methods to identify animals with early stages of OC prevent direct selection pressure eliminate OC from domestic swine herds. Further work to characterize specific candidate genes offers potential tools for future selection programs, but the consequences of selection based on single or multiple candidate genes have not been addressed.

Selection of animals for extremes in growth potential, fat or lean composition, and conformation may indirectly contribute to selection of animals prone to OC disorders. The prevalence of OC disorders expressed across years of genetic progress in selection for production traits would support soundness of these programs, but highlights our need to understand the cellular and genetic basis of OC disorders.

Nutrition

Is overfeeding a problem? In growing animals attempts to alleviate skeletal disorders by over-supplementation of diets with calcium and phosphorus may actually contribute to progression of OC lesions (Crenshaw, 2003). Excess body weight may be a major contributor to the reasons breeding animals are culled for lameness (Wilson et al., 2004).

Attempts to prevent lesions by slowing growth are not economically acceptable and are of questionable benefit. Bone growth and mineralization were not inhibited to the same extent as body weight, when dietary restriction was used to inhibit growth (Crenshaw, 2003). No differences were detected in lameness incidence across various growth rates.

The use of alternate sources of dietary fatty acids to reduce lameness disorders has received attention in humans and animals. Fatty acids are precursors for prostaglandins and may provide anti-inflammatory properties to tissues. In a comprehensive review of fatty acids and arthritis, Darlington and Stone (2001) concluded that sufficient evidence existed to support a beneficial effect of dietary fatty acids for relief of OA symptoms. However, sufficient evidence was not found to support a role of fatty acids in prevention of OA disorders. The primary benefit of elevated n-3 fatty acids was a reduction in inflammatory responses. As such, the n-3 fatty acids have little potential for beneficial roles in earlier stages of OC lesions. Work with neonatal pigs offers some evidence for an improvement in bone mass in pigs fed formula with n-3 fatty acids compared with formula based on n-6 fatty acids (Blanaru et al., 2004).

Ingestion of extracts from shark and or bovine cartilage are purported to alleviate OA and related joint disorders. The active components in these extracts are thought to be glucosamine and/or chondroitin sulfate, both natural compounds derived from cartilage. In a meta-analysis of the research involving efficacy of these compounds for treatment of human OA conditions, McAlindon et al. (2000) found evidence to support only moderate beneficial effects from ingestion of the cartilage extracts. Interestingly, the meta-analysis also detected a publication bias, ie., some published results often made exaggerated claims on the benefits of the extracts. Reports of carefully controlled studies involving glucosamine and swine are not available to my knowledge.

Housing

Stocking rate affected morbidity and mortality in grower/finisher pigs (DeDecker et al., 2005). As stocking rate increased from 22, 27, and 32 pigs per pen (0.78, 0.64 and 0.54 m² per pig) the morbidity and mortality increased from 8.5% to 10.2 and 12.7% respectively. Classifications of the causes for morbidity and mortality were not reported. Are losses associated with overstocking justified?

Disease Prevention and Vaccination Programs

Pathogenic diseases that directly contribute to structural lameness disorders are primarily expressed as an inflammatory arthritis. This condition may be mis-diagnosed as OC, OCD or OA. While no direct link can be identified between disease pathogens and OC, OCD or OA disorders, the potential for exacerbation of pre-existing OC lesions following a disease break must be acknowledged. The indirect complications may arise in animals experiencing trauma associated with weakened condition or compromised housing conditions such as slippery floors following a diarrheal disease.

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