Effects of Nutrition and Gut Barrier Function on the Development of Osteomyelitis Complex and Other Forms of Lameness in Poultry

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Take-Home Message

Poor structural integrity is one potential consequence of gut barrier failure that is often overlooked. Lameness is a significant issue in poultry production. Lameness can manifest itself in a number of ways, including Bacterial Chondronecrosis with Osteomyelitis (BCO), Turkey Osteomyelitis Complex (TOC), and other structural defects such as broken bones and twisted legs. BCO and TOC are among the most common forms of lameness and are associated with opportunistic bacterial infection in the proximal long bone. Some of the bacterial species isolated from BCO and TOC lesions originate in the gut, indicating that the diseases are associated with gut barrier failure. One strategy to reduce incidence of BCO is to improve gut health via probiotics, presumably by enhancing gut barrier function. TOC, which has an immune suppression component, has been shown to be responsive to vitamin D. Depending on the nature of the barrier failure, additional nutritional interventions could include trace minerals and vitamins. Chelated trace minerals have also been shown to positively affect other forms of lameness and structural defects, including reducing the incidence of varus and valgus, tibial dyschondroplasia (TD) and synovitis, as well as increasing bone strength.

Lameness in Poultry

Lameness is common in fast-growing birds in the poultry industry and its incidence within a flock has variably been reported as between 3% and 15% (1) or even more than 15% (2,3). Lameness has increased in association with the rapid increase of growth rate and body weight that has been achieved during the last few decades (4). Male birds are more susceptible to lameness than female birds. Whether lameness is a direct effect of the rapid increase of growth rate and body weight or is an indirect effect of improper development of bone and tendons remains to be determined (4). The important role of gut barrier failure in lameness is suggested by a beneficial effect of probiotic treatment on the incidence of lameness in broilers (5).

Lameness is the fourth cause of economic loss in poultry industry and is estimated to have cost the poultry industry in the U.S. about $120M per year based on the results published in 2000 (6). Lame birds have difficulty in accessing food and water, and can eventually become dehydrated and die (2). The enormous economic losses attributed to lameness in poultry are caused by increases of culls and resultant mortality at farm, condemnations at the processing plant, and further downgrading by the trimming of legs.

Bacterial Chondronecrosis with Osteomyelitis (BCO)

BCO is a metabolic disease with highest incidence in fast growing meat-type chickens. It is recognized as the most common cause of lameness in commercial broilers (2,7-10). A

systematic study in Northern Ireland showed that 17.3% of lame birds had BCO (10). In addition to lame birds, BCO was also identified in birds categorized as "other culls" and "found dead" in the broiler house, and the incidence of BCO was 13.7% of the total deaths and culls and about 0.75% of all birds placed (10,11). BCO has been diagnosed primarily in male broiler chickens in the US, Canada, Australia and Europe. It often causes grossly visible osteomyelitis of the femur, tibia and caudal or fourth thoracic vertebra (12-14) (Figure 1A) and swollen and inflamed hocks (Figure 1B) in broilers and broiler breeders. The onset of clinical signs of lameness in commercial broiler flocks started at about 2 weeks of age, peaked at about 3-6 weeks of age (13,15,16) and most often occurred at 5 weeks of age (10). Lame birds could not stand or move forward and often use their wings (Wing lesion in Figure 1B) for locomotion to reach food and water. The pathogenesis of BCO is hypothesized to be initiated by mechanical damage to poorly mineralized columns of chondrocytes associated with the proximal growth plates of the rapidly growing femora and tibiae (5,17). This is associated with micro-fracture in the growth plate which allows penetration and colonization of opportunistic bacteria in osteochondrotic clefts (5,17). The source of the hematogenous bacteria could be related to barrier failure of gut, skin or respiratory systems.

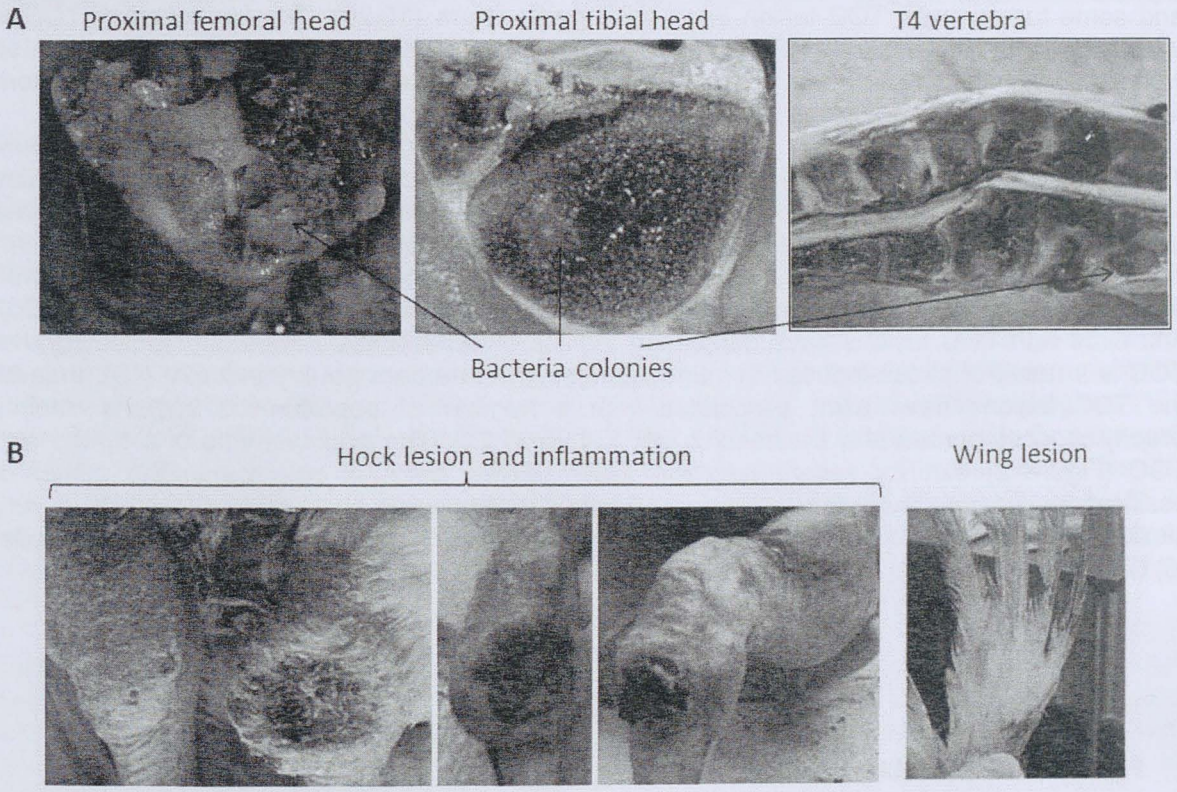


Figure 1. Grossly visible femoral head necrosis, tibial head necrosis, fourth thoracic vertebra osteomyelitis (A), swollen and inflamed hocks and bloody wings (B) in broilers and broiler breeders.

Dr. Robert Wideman and colleagues have developed a reliable model to induce a high incidence of lameness in broilers by raising broilers at relatively low densities in large wire flooring pens and allowing normal levels of activity (5,17). In this model the wire is elevated to permit manure to pass through. Feed is provided at one side of pen and water is provided at the

opposite side of pen, forcing the birds to walk cross the pen to eat and drink. The resulting footing instability on the wire causes constant additional mechanical torque and shear stress on susceptible leg joints, and reproducibly induces a substantial incidence of lameness. Almost all of the lame birds developed BCO with femoral and/or tibial head necrosis in one leg or both legs, some of them were infiltrated by bacterial colonies. In addition, deprivation of litter in the wire flooring pen may cause chronic stress including immunosuppression for the birds (18), which might partially contribute to the high incidence of lameness (5). This wire flooring model allows researchers to investigate the etiology, pathology, prevention and intervention strategies of BCO and lameness in broilers.

Turkey Osteomyelitis Complex (TOC)

TOC is a disease characterized by lesions that include proximal tibial osteomyelitis, arthritis and synovitis, and abscess in soft tissue of leg and breast. It is found in the carcasses of processed turkeys that may outwardly appear to be healthy (19). The birds with TOC usually have green livers, so green liver has been used as an indicator for TOC by the USDA inspection program. This can be misleading, however, because only 50% turkeys with green liver have TOC lesions and some turkeys with TOC lesion don't have green livers (19,20). The incidence of TOC is usually low with 0.13-1% turkeys having green liver (19), however, the mortality rate associated with leg problems including lameness, bone developmental disorders and bone fracture in tom flocks can be as high as 5% of a flock (21,22).

TOC is very similar in pathology to BCO. TOC primarily affects male turkeys but not females (23-25). The birds with TOC generally develop lameness and eventually die usually in their late growth phase when producers have already spent a large amount of money in their production. Therefore, the economic loss due to TOC is high. TOC can be induced experimentally with dexamethasone (DEX), a synthetic glucocorticoid that can induce immune suppression (26), and birds with TOC lesions have decreased indices of cell-mediated immunity, indicating that TOC is a result of stress-induced immunosuppression in modern poultry industry (19). Indeed, the TOC lesions have been associated with a number of opportunistic bacteria, mainly *Staphylococcus aureus* and *Escherichia coli* (24,25,27,28). The proximal tibia of a turkey with TOC (Figure 2) exhibits severe necrosis with caseous bacterial colonies in the center of ossification and the secondary site of ossification in the epiphysis (Figure 2), which is very similar to the tibial head necrosis in broiler chickens with BCO seen in the wire flooring model (5) (Figure 1A).

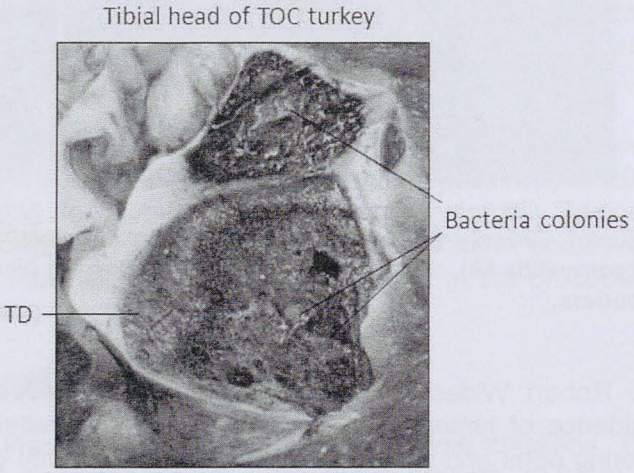


Figure 2. Proximal tibial head necrosis in turkeys with TOC.

Other Forms of Lameness

In addition to BCO and TOC, twisted legs such as varus and valgus deformity (29-31) and TD (29,30,32,33) have been recognized as the causes of lameness in poultry (Figure 3). Synovitis (Figure 3) has also been reported to be associated with lameness (24,34).

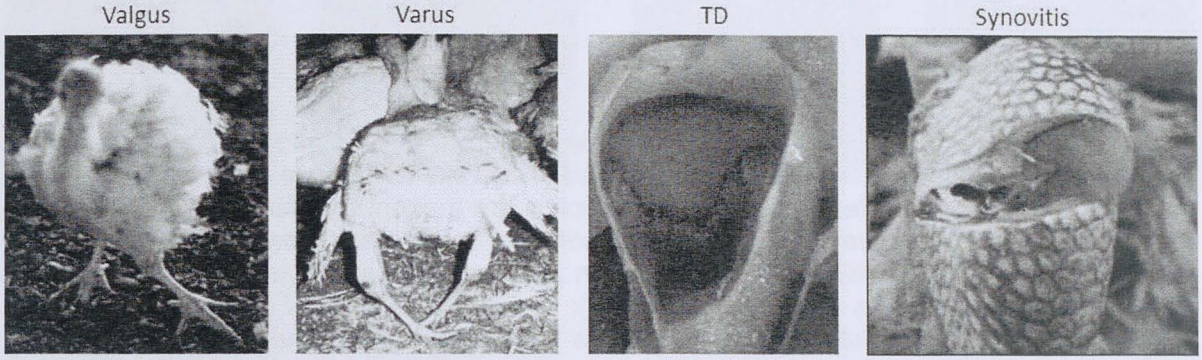


Figure 3. Other forms of lameness in poultry including valgus, varus, TD and synovitis.

Gut Barrier Failure Attributed to BCO and TOC

There is compelling evidence showing that the bacteria associated with BCO and TOC can originate from the gut. Enterococci are normal commensal bacteria in the gastrointestinal tract of birds and mammals and are also opportunistic bacteria that can cause disease in poultry and in humans (12,16,35). *Enterococcus (E.) spp* have been reported to be involved in femoral head necrosis in chickens (10). *E. cecorum* was isolated from the lesions of osteomyelitis of the caudal thoracic vertebrae, hock joints or femur in affected broilers and broiler breeders suffering from vertebral osteomyelitis, chondronecrosis, or femoral head osteomyelitis in Belgium (16), Netherlands (36), Canada (13), Scotland (37), Holland (38) and the USA (39). *E. hirae* was identified to be the primary cause of osteomyelitis in lame chickens in Norway (15). *E. faecalis* and *E. faecium* were isolated from femoral head necrotic lesions of chickens in Turkey (40). In addition to enterococci, other bacteria were also isolated from birds with osteomyelitis, such as *Staphylococcus aureus* (40), *Escherichia coli* (39,40), *Salmonella* spp (41), *Staphylococcus* sp and *Proteus* sp. (39).

Similar to BCO, enterococcus species, as well as *Staphylococcus aureus* and *Escherichia coli*, have also been isolated from the livers and bone lesions of birds with TOC (19). A longitudinal study of green-liver osteomyelitis complex in commercial turkeys at two farms found that both farms had high incidence of intestinal lesions (27). These findings suggest that TOC may be associated with gut barrier failure.

Taken together, the data indicate that vertebral osteomyelitis, BCO and TOC are all associated with opportunistic pathogens of gut origin and that gut barrier failure is a predisposing factor responsible for the bacterial infection in the bone of poultry with osteomyelitis.

Prevention and Intervention Strategies to Alleviate Osteomyelitis Complex and Lameness in Poultry

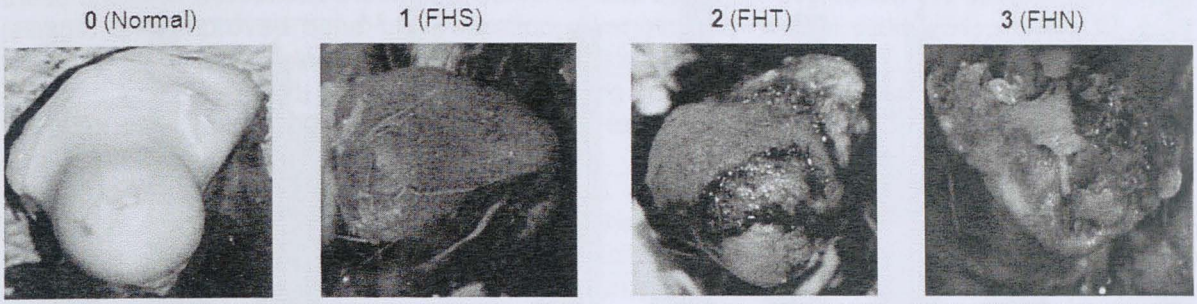
Lameness in poultry can be caused by BCO, TOC, bone weakness, leg deformity, tendon rupture, TD, synovitis and rickets. The potential prevention and intervention strategies to alleviate the incidence of osteomyelitis complex and other forms of lameness in poultry are summarized below.

1. Probiotics

Probiotics are live, beneficial and nonpathogenic bacteria that can modify and balance the composition of intestinal microflora, and provide an alternative to improve gut health, especially as antibiotic growth promoter use declines. Probiotics are thought to alter intestinal microbiota through several different ways: 1) Inhibition of pathogenic bacterial growth by releasing antimicrobial substances (42-46); 2) Competition with pathogens for available nutrients (46,47); 3) Production of lactic acid as an antimicrobial (48); and 4) Modulation of immune response by increasing production of antibodies and cytokines (46,49-51). As a result, gut barrier function can be improved with probiotics.

Previous work has shown that probiotics can reduce the incidence of BCO and proximal tibial head lesions (5). In our recent trial, we tested the efficacy of SPORULIN®, a direct-fed spore-based *Bacillus* probiotic, in reducing the symptoms of BCO related lesions using a model based on that described by Wideman (5). The proximal femoral head and tibial head lesions were diagnosed and scored for % incidence and severity as described by Wideman and colleagues (5,52) (Figure 4). The severity of bone lesions of birds at 57-58 days of age is shown Figure 5A and B, and percent incidence of lesions is shown in Figure 5C and D. We found that the probiotic decreased the lesion severity of right femoral heads, tibial heads and total legs (average lesion score of femoral heads and tibial heads) in all necropsied birds including non-lame and lame birds (Figure 5A). Lame birds had worse score of femoral heads and tibial heads compared to normal (non-lame) birds (Figure 5B). The reduction of femoral head and tibial head lesion score by probiotic treatment was slightly lesser than but comparable to the differences of lesion scores between normal and lame birds, suggesting that the probiotic is an effective solution to attenuate bone lesions. Probiotic treatment also numerically decreased the percentage of total tibial head lesions (THN+THNs+THNc) in all day 57-58 birds necropsied ($p<0.08$, Figure 5C). This effect was attributed to a significant increase in normal tibias in the non-lame birds (Figure 5D). These results suggest that SPORULIN® can attenuate lameness-related symptoms (particularly tibial head necrosis in this trial) presumably by improving gut barrier function thereby decreasing the possibility of bacteria escaping the gut into the bloodstream, and penetrating into the growth plate of femurs and tibias. These findings further support that gut health plays an important role in BCO and related lameness.

Femoral head lesion score:



Tibial head lesion score:

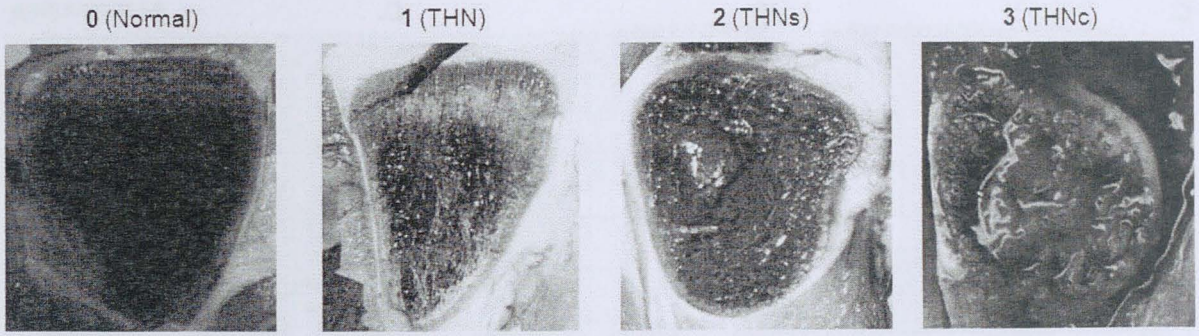


Figure 4. Scoring of proximal femoral head and tibial head lesions of broilers reared on wire flooring.

The proximal femoral heads were evaluated and scored as described below.
Score 0: normal, macroscopically normal femur without apparent abnormalities;
Score 1: FHS, femoral head separation;
Score 2: FHT, femoral head transitional degeneration;
Score 3: FHN, femoral head necrosis.

The proximal tibial heads were evaluated and scored as below:
Score 0: normal, no apparent abnormalities;
Score 1: THN, mild proximal tibial head necrosis without damage in growth plate;
Score 2: THNs, severe THN in which the growth plate was imminently threatened or damaged;
Score 3: THNc, severe THN in which caseous exudates or bacterial sequestrae were macroscopically evident.

Scoring system was based on that described by Gilley (52).

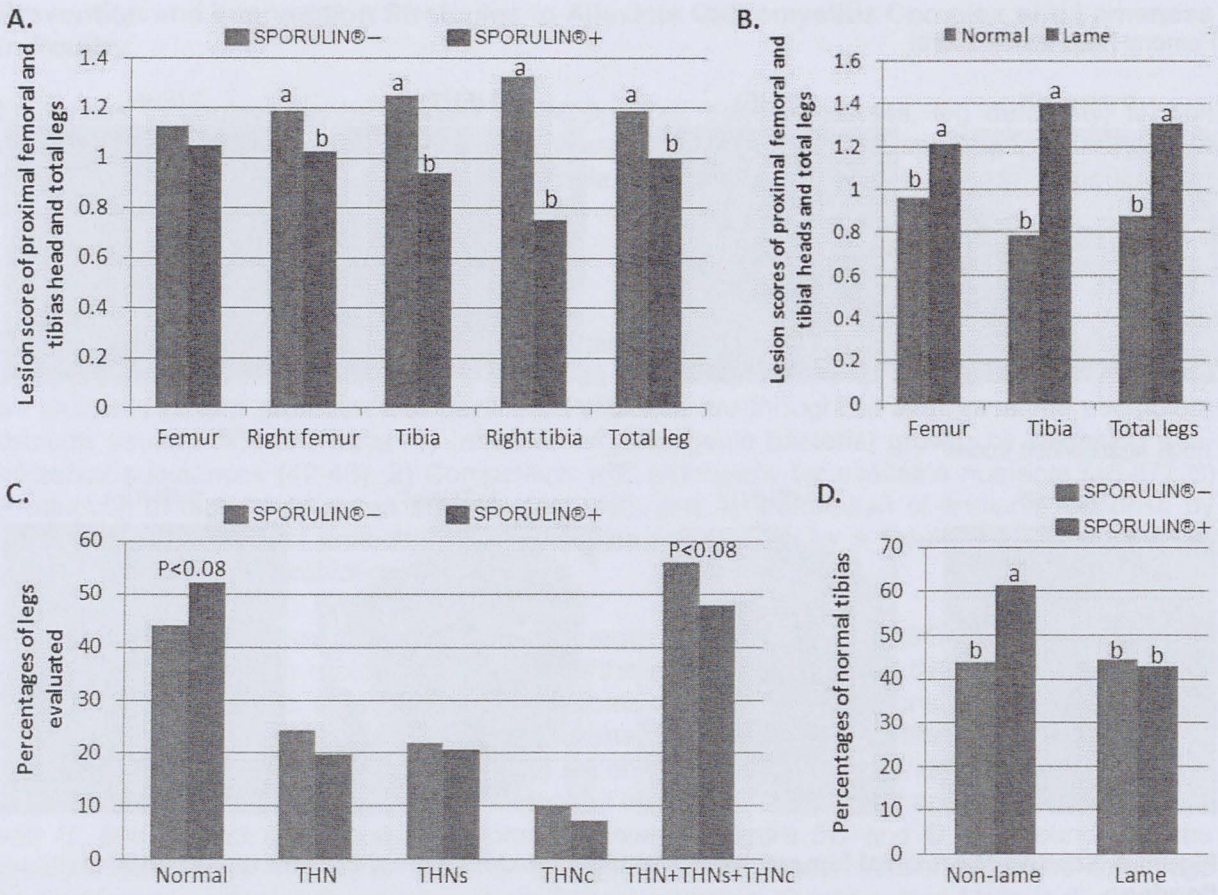


Figure 5. Efficacy of SPORULIN® in the alleviation of proximal tibial head lesions in broilers reared on wire floor. A. Lesion scores of proximal tibial head of birds treated with (+) or without (-) SPORULIN®. The score of total legs is the average score of femoral heads and tibial heads. B. Lesion scores of proximal tibial heads in normal (non-lame) and lame birds. C. Percentages of normal tibial heads (Normal), THN, THNs, THNc and total tibial head lesions (THN+THNs+THNc) in birds treated with (+) or without (-) SPORULIN®. D. Effect of lameness and SPORULIN® on the percentage of normal tibias.

2. Trace minerals

Trace minerals play a very important role in bone and skeletal development and joint health. Zn promotes collagen synthesis and turnover in developing bone. Cu is essential for cross-linking of collagen and elastin, and adequate Cu intake is important to obtain peak bone mass in long bones and to prevent femoral bone fractures. Manganese (Mn) is an essential element for bone and tendon development as Mn deficiency causes tibial twisting and bending, tibiometatarsal joint enlargement and malformation, resulting in slippage of the gastrocnemius tendon from its condyles (53). It is also associated with shorter and thicker long bones in poultry (53). Therefore, Zn, Cu and Mn are supplemented in virtually all livestock diets either as inorganic trace mineral (ITM) salts or organic trace minerals (OTMs) or a combination of both. Fast growing birds may need higher levels and/or more bioavailable forms of minerals to obtain optimal bone development and joint health (54). OTMs have the potential to be more bioavailable than ITMs (55-59), and a number of studies showed that MINTREX®Zn, Cu and Mn (the chelated trace minerals referred to below) have higher bioavailabilities than ITM or other forms of OTM (58-60).

We hypothesized that inclusion of these chelates into diets could improve structural health in poultry. Indeed, in a commercial turkey trial in flocks that exhibited symptoms of TOC (Figure 2), these chelates decreased the incidence of TD and synovitis, decreased the severity of footpad lesions, and improved bone mineralization, strength and cortical width (54) (Figure 6). In a follow-up study conducted at North Carolina State University, dietary supplementation of these chelates and selenized yeast partially replacing the existing mineral premix, increased tibia breaking strength in turkeys, especially when fed in combination with 25-hydroxyvitamin D3 (HyD) in a commercial trial (Figure 7A) (31). These OTMs also significantly reduced the incidence of lameness including valgus, varus and shaky legs in turkeys (Figure 7B) (31). Finally, these chelated trace minerals reduced the incidence of femoral head lesions of broilers reared on wire flooring (data not shown). Collectively, these findings indicate that MINTREX® OTM is an effective organic trace mineral source to satisfy the trace mineral needs of fast growing broilers, improve structural health of bone, joint and footpad, and reduce the incidence of lameness in poultry.

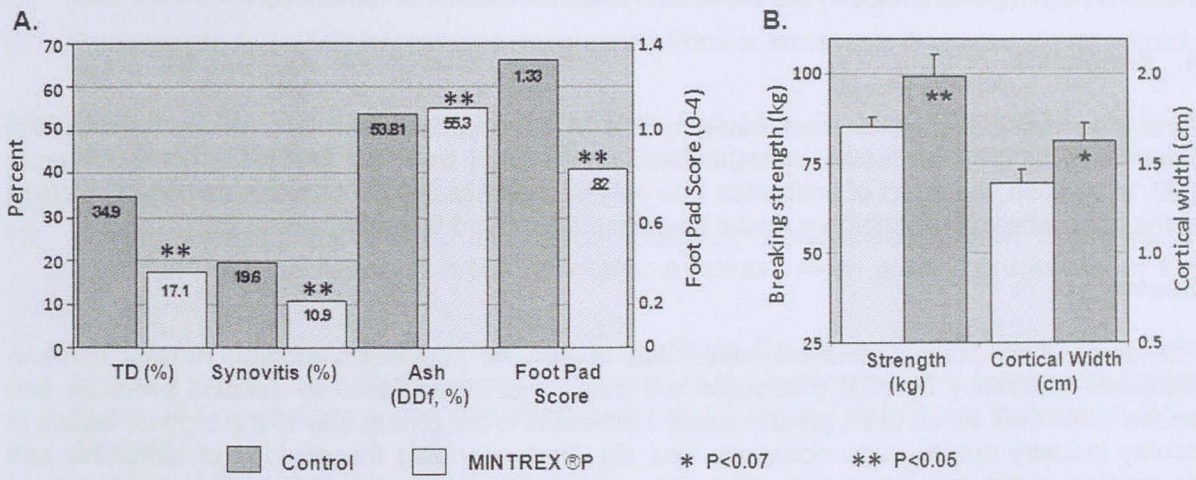


Figure 6. Effect of MINTREX® P on the incidence of TD, synovitis, tibial ash content, footpad score (A), breaking strength and cortical width (B) in turkeys.

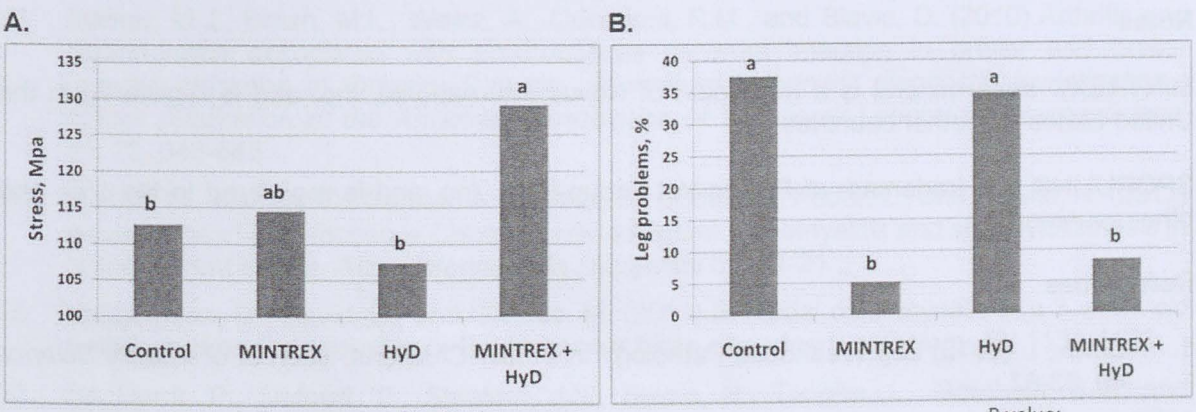


Figure 7. Effect of MINTREX® PSe and HyD on tibial breaking strength (A) and the percentages of total leg problems (B) in turkeys.

3. Vitamins

Numerous studies described the involvement of vitamins in the skeletal development of poultry. Vitamin D and its metabolites are by far the most studied factors in relation to bone disorders (61). Vitamin D3 is important in Ca and P absorption and metabolism, and its deficiency causes a reduction in mineralization of growing bones potentially leading to weak legs, rickets and lameness (62). The vitamin D3 metabolite, HyD, when fed in combination with MINTREX® PSe increased tibia breaking strength in turkeys (31) (Figure 7), which may decrease the opportunity for bacteria to penetrate into the bone and thereby help to improve bone structural health. Supplementation with vitamin D3 or HyD protected turkeys from the immunosuppressive effects of multiple DEX treatments and decreased the incidence of TOC in turkeys (23,63). Supplementation of high dietary levels of vitamin D3 also decreased the incidence and severity of TD in broiler chickens (23,64,65). Vitamins D and B12 deficiency in human lead to rickets with severe hypocalcemia, femoral epiphysiolysis and eventually lameness (66). In summary, vitamins play important roles in the prevention and intervention of lameness.

4. Antibiotics

Antibiotics can be used to treat osteomyelitis in poultry, however, in one study, antibiotic treatment was only successful when initiated preventively from the first week of life onwards (16). In addition, the effect of antibiotics was only partial because the bacteria can often colonize in the bone where any antibiotics would have insufficient and limited access (36).

Summary

The demand for poultry meat increases due to general population growth. As this demand increases, efficiency of meat production will also have to increase, so disease pressure and animal health will be an even greater issue. Lameness is becoming one of the biggest issues in poultry industry due to huge economic loss (6). Understanding the etiology of lameness and developing nutritional prevention and intervention strategies to reduce the incidence of osteomyelitis and lameness and to alleviate lameness symptoms are becoming more and more important and urgent with the passing of time.

Notes

MINTREX® trace mineral is a trademark of Novus International, Inc. and is registered in the United States and other countries

SPORULIN® is a trademark of Pacific Vet Group-USA, Inc. and is registered in the U.S. and other countries.

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