

Turkey Osteomyelitis Complex

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ABSTRACT Turkey osteomyelitis complex (TOC) is defined by the US Food Safety Inspection Service (FSIS) to include normal-appearing processed turkey carcasses that contain lesions including green discoloration of the liver, arthritis/synovitis, soft-tissue abscesses, and osteomyelitis of the proximal tibia. The lesions are associated with many different opportunistic organisms, mainly *Staphylococcus aureus* and *Escherichia coli*, suggesting that TOC incidence may be influenced more by deficiencies in the host immune response rather than by the virulence of any one organism. This syndrome is primarily a disease of adolescent male turkeys, and birds with TOC lesions have decreased indices of cell-mediated immunity, leading to the hypothesis that defects in the immune response of individuals within flocks of male turkeys may be responsible for the occurrence of these opportunistic infections. We have developed an experimental model for this disease in which treatment with dexamethasone (DEX), either with or without air sac inoculation with *Escherichia coli*, produces all of the lesions associated with TOC. These studies suggest that TOC is a result of stress-induced immunosuppression in a subpopulation of male turkeys

that respond to the stressors in modern poultry production in a detrimental manner. Supplemental vitamin D₃ treatment protected male turkeys from the immunosuppression induced by multiple treatments with DEX and resulted in decreased incidence of mortality, TOC, green liver, and isolation of bacteria from tissues, lower air sacculitis scores, and lower heterophil to lymphocyte ratios than nonsupplemented controls. Vitamin D₃ also protected BW; relative weights of the liver, heart, spleen, and bursa; and clinical chemistry values from the effects of DEX treatment. The ability of vitamin D₃ supplementation to protect turkeys from the immunosuppressive effects of severe stress emphasizes its role as a prohormone that affects health and disease resistance in turkeys and suggests that variation in the vitamin D receptor genotype may be involved in this disease process. This model has potential value in the identification of other nutritional and physiological immunomodulators that can decrease TOC incidence and will provide a means for the divergent selection of birds more resistant to the stressors of turkey production. In addition, this model will provide justification for management options designed to minimize stress.

(Key words: turkey osteomyelitis complex, stress, vitamin D, dexamethasone)

2000 Poultry Science 79:1050–1056

INTRODUCTION

In 1988, USDA Food Safety Inspection Service (FSIS) veterinarians in an Arkansas turkey processing plant noticed a correlation between the presence of green livers in turkeys and various internal lesions, including arthritis/synovitis, soft-tissue abscesses, and osteomyelitis of the proximal tibia. The FSIS became concerned mainly because *Staphylococcus aureus*, a potential human pathogen, was isolated from many of the lesions, and the carcasses containing these lesions appeared to be healthy by external examination. Studies conducted by the FSIS showed that this condition was present in about half of the turkeys that had green discolored livers at processing (McCaskey,

1989). Thus, the FSIS began a mandated federal inspection procedure that requires that the first 10 birds with green livers from each lot of birds processed be hung in a special area and cut with a standard 10-cut procedure to inspect for abscesses, synovitis, and osteomyelitis of the proximal tibia. If any green liver birds from this sample exhibit any of these lesions, then all birds with green livers from that lot must be cut (Cook, 1988). This procedure generally results in the downgrading of all green-liver turkeys by using the 10-cut procedure. The FSIS feels that this inspection procedure is necessary to prevent these unwholesome and potentially dangerous carcasses from reaching the consumer.

Green livers were found to occur in 0.13% of turkey hens and 0.65% of toms processed in the Southeastern

Received for publication December 15, 1999.

Accepted for publication February 29, 2000.

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Abbreviation Key: DEX = dexamethasone; FSIS = USDA Food Safety Inspection Service; TD = tibial dyschondroplasia; TOC = turkey osteomyelitis complex; VDR = vitamin D receptor.

United States (Barnes et al., 1993). A second study of 42,010 inspected turkeys from seven commercial farms in the same area found the average green liver incidence to be 0.69%, (hens, 0.14% and toms, 1.04%) (Mutalib et al., 1996). The current inspection system results in nearly all of these turkeys being cut and downgraded; however, only about 50% of the turkeys with green livers have turkey osteomyelitis complex (TOC) lesions (McCaskey, 1989; Barnes et al., 1990; Tilley and Barnes, 1990; Clark et al., 1991; Bayyari et al. 1994; Mutalib et al., 1996). The turkey industry has protested that this inefficient screening process costs many millions of dollars in lost time and product and would like to find a better method for removing these turkeys from the food chain. In addition, TOC lesions have been detected in carcasses that do not have green livers (Bickford et al., 1990; Clark et al., 1991; Bayyari et al., 1994). Therefore, the use of green liver as an indicator for TOC may be as inefficient for FSIS inspection as it is costly to the turkey industry.

Our laboratory has been interested in understanding why a small, but stable, proportion of otherwise healthy-appearing turkeys develop these opportunistic infections. An initial investigation into the etiology of TOC was undertaken to understand the pathogenesis of the disease, including the nature of the organisms involved, the natural route of exposure and initial portal of entry, the progression of clinical signs, and the age at which the lesions could first be detected.

TOC Field Study

One hundred turkeys were necropsied weekly throughout a 15-wk growout, randomly sampling 50 turkeys weekly from each of two Arkansas farms that historically had a relatively high incidence of TOC (Bayyari et al., 1994). These flocks came from the same breeder flock but from different hatcheries and were set within 1 d of each other. They were raised using the same diets, supplements, medications, and management practices recommended by the integrator. The TOC lesions did not appear until Week 9 of the growout and increased steadily through Week 15. There was a similar pattern in the incidence and severity of tibial dyschondroplasia (TD), which increased from 4% at 10 wk of age to 81% at 15 wk of age (Rath et al., 1994). There was no difference in TD incidence between the two farms. However, Farm B had a higher incidence of TOC and green liver and also had higher early and weekly mortality, air sacculitis incidence, and seroconversion to *Mycoplasma meleagridis* and Newcastle disease virus. This farm practiced a three-house management system, moving birds at 5 wk and 12 wk of age, whereas the farm with the lower disease incidence kept the birds in a single house throughout the growout. Birds from both farms had a high incidence of enteritis and infestation with *Ascaridia dissimilis*. Thus, it appeared that TOC may be related to chronic respiratory infection and the stresses inherent in both management practices and disease.

L-Form Bacteria

Although *S. aureus* was isolated from many of the livers and lesions of birds with TOC, other opportunistic bacteria, such as *Escherichia coli* and enterococcus species were also isolated. The isolation of many different bacterial species from these lesions has been reported (Wise and Uppal, 1972; Nairn, 1973; Barbour et al., 1991; Clark et al., 1991; Bland et al., 1993; Tate et al., 1993; Droual et al., 1996; Mutalib et al., 1996). The use of more intensive methods of culturing, such as decreasing the amount of oxygen, using longer incubation times, and utilizing hypertonic and serum-supplemented media, resulted in the isolation of bacteria from nearly all samples cultured. In previous studies, bacteria were isolated from an average of 40% of the liver, bone, and joint lesions cultured (Clark et al., 1991). A slow-growing, pleomorphic microbe was isolated from most of the lesions that had appeared sterile and was cultured using extended incubation and hypertonic medium. After trying to identify this organism as an actinomyces sp. based on its morphology, it was found that these were actually the L-forms or cell-wall deficient forms of the same common, opportunistic bacterial species found in the lesions (Bayyari et al., 1994). L-form bacteria are known to grow inside red and white blood cells, and it is thought they may be more prevalent in animals with a low immune response (Khorany and Kendrick., 1966; Mattman, 1993). We therefore hypothesized that there may be a deficiency in the ability of the green liver turkeys to kill phagocytosed bacteria.

Host Immune Response, Genetics, and TOC

Various parameters of the immune systems of birds with and without TOC were tested in a relatively small sample of birds with and without TOC (Bayyari et al., 1997a). There were no differences in phagocytosis or bacterial killing of both monocytes and heterophils, but there was a significant decrease in the function of the T-cell mediated immune response of the TOC birds, an increase in complement levels, and an increase in the heterophil/lymphocyte ratio, which is a standard measure of stress in birds (Gross and Siegel, 1983). Differences in the immune response of different genetic strains of turkeys were also studied (Bayyari et al., 1997b). Turkeys selected for faster growth had a decrease in some responses, including cutaneous basophil hypersensitivity response, and an increase in others as compared with their parent stock. In the same study two commercial turkey lines were also compared, and the line having a faster early growth rate also had decreased cutaneous basophil hypersensitivity.

DEXAMETHASONE IMMUNOSUPPRESSION AND TOC

Dexamethasone (DEX) is a synthetic glucocorticoid that has been reported to decrease the cutaneous basophil hypersensitivity response (Corrier and DeLoach, 1990),

TABLE 1. Experiment 1. Effect of dexamethasone (DEX) injection and *Escherichia coli* respiratory challenge on the incidence of turkey osteomyelitis complex (TOC)¹

<i>E. coli</i> cfu ²	TOC Incidence ³	
	With DEX	No DEX
0	8.33 ± 5.76 ^b	0.00 ± 0.00 ^b
2	27.08 ± 6.48 ^a	7.41 ± 5.1 ^{ab}
3	23.64 ± 5.78 ^a	3.23 ± 3.23 ^b
4	20.37 ± 5.53 ^a	0.00 ± 0.00 ^b
5	10.71 ± 4.17 ^b	22.22 ± 8.15 ^a

^{a,b}Means with no common superscript are significantly different ($P \leq 0.05$).

¹Data are from Bayyari *et al.*, 1994.

²Inoculum was diluted in tryptose phosphate broth so that a 200- μ L injection contained 0 or approximately 10^2 , 10^3 , 10^4 , or 10^5 cfu of a pathogenic strain of *E. coli*.

³Values indicate the mean \pm SE of all mortalities and either 10 necropsied birds from each pen or all of the surviving birds from each pen having less than 10 survivors.

induce cell-mediated immunosuppression, and decrease resistance to coccidiosis (Isobe and Lillehoj, 1992, 1993) in chickens. It has been used to induce immunosuppression in a model of transport stress of cattle (Roth and Flaming, 1990). Dexamethasone has many wide-ranging effects on the immune system and has been shown to increase the incidence of opportunistic infection due to its ability to interfere with the bactericidal activity of macrophages (Schaffner, 1985; Schaffner and Schaffner, 1988, Huff *et al.*, 1999c). We have developed an experimental model for reproducing TOC lesions based on the hypothesis that a small percentage of male turkeys react to the stresses of modern poultry production in a deleterious manner, sustaining high glucocorticoid levels and becoming immunosuppressed. The following experiments demonstrate the efficacy of this model in reproducing TOC using pharmacological doses of DEX.

Experiment 1

Dexamethasone treatment was used in combination with air sac inoculation with various amounts of *E. coli* in order to increase TOC incidence (Huff *et al.*, 1998a). Six-hundred 5-wk-old male turkeys were given three intramuscular injections of 2 mg DEX/kg BW on alternating days or were untreated. On the day of the third DEX injection, the left thoracic air sac of each bird was injected with sterile tryptose phosphate broth (TPB; 1×10^0) or with tryptose phosphate broth containing 1×10^2 , 1×10^3 , 1×10^4 , or 1×10^5 cfu of *E. coli*. All mortalities and birds necropsied at 2 wk postinoculation were examined for lesions of TOC, following the standard 10-cut procedure used by the FSIS, and were scored for air-sacculitis/pericarditis on a scale of 1 to 5 using a modification of the scoring system described by Piercy and West (1976).

Dexamethasone treatment, by itself, increased TOC incidence from 0 to 8%, and there was a synergistic interaction between DEX treatment and *E. coli* challenge ($P = 0.06$) (Table 1). Although TOC incidence was significantly increased by the lowest level of *E. coli* inoculated (1×10^2

TABLE 2. Experiment 2. Effect of a second dexamethasone (DEX) injection on turkeys previously challenged in a DEX-*Escherichia coli* respiratory infection on the incidence of turkey osteomyelitis complex (TOC)¹

<i>E. coli</i> cfu ²	TOC lesions ³	
	No DEX	DEX
0	6.25 ± 6.25	63.64 ± 15.21 ^a
25	0.00 ± 0.00	42.86 ± 13.73 ^{ab}
50	10.00 ± 6.88	20.00 ± 20.00 ^b
Probability values		
DEX	0.0001	
<i>E. coli</i>	0.1516	

^{a,b}Means with no common superscript are significantly different ($P \leq 0.05$).

¹Data are from Huff *et al.*, 1999b.

²Inoculum was diluted in tryptose phosphate broth so that a 200- μ L injection contained 0, 25, or 50 cfu of a pathogenic strain of *E. coli*.

³Values indicate the mean \pm SE of all mortalities and necropsied birds.

cfu), increasing the number of bacteria did not increase TOC incidence due to high mortality before TOC lesions developed. There was no increase in TOC incidence in non-DEX-treated birds treated with less than 1×10^5 cfu of *E. coli* (Table 1).

Experiment 2

Lower levels of *E. coli* were used to reduce mortality, and DEX treatments were given at age 5 wk and again at age 12 wk of age (Huff *et al.*, 1999b). Three hundred forty-eight 5-wk-old male turkeys were treated with DEX injections followed by air sac inoculation with 0, 25, or 50 cfu of *E. coli* as previously described. Survivors of this challenge were maintained until 12 wk of age, at which time they were treated with a second series of DEX injections. Mortalities and birds necropsied 3 wk after the second DEX injection were examined for air sacculitis and TOC lesions.

The second series of DEX injections resulted in 64% incidence of TOC (Table 2) and green liver (Table 3);

TABLE 3. Experiment 2. Effect of a second dexamethasone (DEX) injection on turkeys previously challenged in a DEX-*Escherichia coli* respiratory infection on the incidence of green liver¹

<i>E. coli</i> cfu ²	Green liver ³	
	No DEX	DEX
0	0.00	63.64 ± 15.21 ^a
25	0.00	21.43 ± 11.38 ^b
50	0.00	26.32 ± 10.38 ^b
Probability values		
DEX	0.0001	
<i>E. coli</i>	0.0061	

^{a,b}Means with no common superscript are significantly different ($P \leq 0.05$).

¹Data are from Huff *et al.*, 1999b.

²Inoculum was diluted in tryptose phosphate broth so that a 200 μ L injection contained 0, 25, or 50 cfu of a pathogenic strain of *E. coli*.

³Values indicate the mean \pm SE of all mortalities and necropsied birds.

TABLE 4. Experiment 3. Effect of sequential dexamethasone (DEX) treatments on the incidence of green liver (GL) and turkey osteomyelitis complex (TOC) lesions in mortalities and necropsied turkeys never inoculated with *Escherichia coli*

	No DEX		DEX	
	TOC	GL	TOC	GL
First DEX Age: 2 wk	ND ¹	ND	ND	ND
Second DEX ² Age: 5 wk	0/30	0/30	26/96 (27%)	8/96 (8.3%)
Third DEX ³ Age: 10 wk	2/41 (4.9%)	1/41 (2.4%)	33/49 (67%)	17/49 (35%)

¹ND = not done. There was no mortality or lameness after the first DEX treatment.

²There was no mortality in non-DEX-treated birds. There were 46 mortalities and 50 necropsied birds in the DEX-treated group, and percentages include all mortalities and necropsied birds.

³There was 1 mortality and 40 necropsied birds in non-DEX-treated birds. There were 38 mortalities and 11 necropsied birds in the DEX-treated group. Percentages include all mortalities and necropsied birds.

however, birds previously inoculated with 50 cfu of *E. coli* had a lower incidence of green liver and TOC compared to birds only treated with DEX. We believe that this result occurred because the birds most susceptible to the DEX-*E. coli* challenge died after the first DEX treatment, leaving a more resistant population. There were no mortalities of birds given a single DEX treatment and not challenged with *E. coli* (data not shown).

Experiment 3

Seven-hundred twenty male turkeys were treated with DEX at 2 wk of age or were untreated. Because there was no mortality or evidence of lameness, no birds were necropsied. At 5 wk, the DEX-treated birds were given a second DEX treatment. All mortalities were examined for air sacculitis and TOC lesions. Two weeks later, 30 control and 50 DEX-treated birds were necropsied. The birds that survived were raised until 10 wk of age, at which time all DEX-treated birds were given a third DEX treatment. All mortalities were examined for air sacculitis and TOC lesions and 2 wk after the 3rd DEX treatment, the survivors were necropsied.

There was no mortality due to DEX treatment of birds treated at 2 wk of age. Mortality increased with age and number of DEX treatments, with 32% mortality at 5 wk of age (after two DEX treatments) and 79% mortality at 10 wk of age (after three DEX treatments). There was no evidence of lameness in birds treated with DEX at 2 wk of age, therefore no birds were necropsied. There was no incidence of either TOC or green liver in non-DEX-treated birds at 5 wk of age; however, 5-wk-old DEX-treated birds had 27% TOC and 8.3% green liver after the second DEX treatment (Table 4). There was 4.9% TOC and 2.4% green liver in 10-wk-old non-DEX-treated birds, whereas 10-wk-old birds given three DEX treatments had 67% TOC and 35% green liver (Table 4).

Gender and Stress

Turkey osteomyelitis complex is a disease that primarily affects male turkeys between 9 and 20 wk of age and is not a significant problem in females (Nairn, 1973; Clark et al., 1991; Mutalib et al., 1996), suggesting that known differences in the stress response between males and females (Homo-Delarche et al., 1991) may be involved in its etiology. The immunosuppressive effects of DEX treatment appear to be greater in male birds than in females (Huff et al., 1999a). We have reported that female turkeys are more resistant to colisepticemia in the DEX-*E. coli* challenge than are males; however, this study failed to produce high TOC incidence in either males or females. Retrospective analysis of the conditions of this study determined that the low TOC incidence might be due to the supplementation of these poult with water-soluble vitamin D₃ for the first week of life. This treatment was used in an effort to prevent field rickets, which is a sporadic problem in our facilities.

VITAMIN D₃ SUPPLEMENTATION AND TOC

We have used the DEX model to evaluate the ability of supplemental vitamin D₃ to protect male turkeys from the immunosuppressive effects of severe stress (Huff et al., 1998b). All poult were maintained on a standard corn-soy turkey starter diet that met or exceeded the nutrient requirements established by the NRC (1994). The feed was formulated with a vitamin premix calculated to provide 2,204 IU of vitamin D₃/kg. Treated poult were supplemented with an additional 2,064 IU vitamin D₃²/L in drinking water ad libitum during the first 5 d of brooding and again at a higher level (4,128 IU/L) before, during, and after each stressful event, which we defined as weekly weighings and DEX challenges. Vitamin D₃ supplementation had no effect on disease resistance, hematology values, or body and organ weights of birds that were treated with DEX at 5 wk of age and necropsied 2 wk later. However, vitamin D₃ supplementation did significantly decrease mortality, TOC incidence, green liver incidence, and the recovery of bacteria from the liver and air sacs

²High D, I.D. Russell Company Laboratories, Longmont, CO 80501.

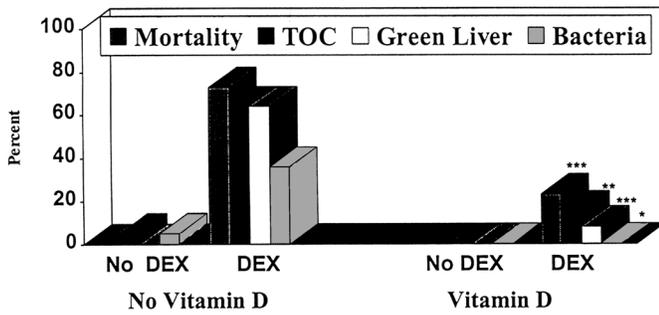


FIGURE 1. The effect of vitamin D₃ supplementation on mortality, incidence of turkey osteomyelitis complex (TOC) lesions, incidence of green liver discoloration, and isolation of bacteria from tissues of 14-wk-old male turkeys treated with dexamethasone (DEX) at 5 wk and again at 12 wk of age. Differences between vitamin D treatments at **P* = 0.01, ***P* = 0.001, and ****P* = 0.0001.

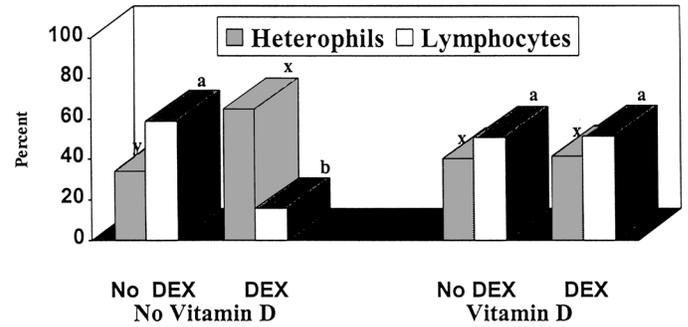


FIGURE 3. The effect of vitamin D₃ supplementation on the mean percentage of heterophils and lymphocytes in the peripheral blood of 14-wk-old male turkeys that were treated with dexamethasone (DEX) at 5 wk and again at 12 wk of age. ^{a,b,x,y}Values within each cell type with no common superscript differ significantly. Heterophil *P*-value = 0.006; Lymphocyte *P*-value = 0.0001.

of survivors of the first treatment that were treated with DEX again at 12 wk of age (2X-DEX; Figure 1). Air sacculitis scores were fourfold higher in 2X-DEX-treated birds not given supplemental vitamin D₃ (*P* = 0.0002; Figure 2). The DEX injection increased the percentage of heterophils and decreased the percentage of lymphocytes in the peripheral blood of birds not given supplemental vitamin D₃; however, 2X DEX-treated birds given supplemental vitamin D₃ were protected from these changes (Figure 3). Vitamin D₃ supplementation also protected against DEX-induced loss of body weight in 2X DEX-treated turkeys (*P* = 0.0005) (Figure 4).

DISCUSSION

The DEX model reproduces all of the lesions associated with TOC, including green liver, arthritis/synovitis/tenosynovitis, abscesses in soft tissues, and osteomyelitis of the proximal tibia. These results support our hypothesis that the TOC problem is not due to the pathogenicity of any single organism but is related to stress-induced immunosuppression in a subpopulation of male turkeys that respond to the stressors of modern turkey production in an inappropriate and detrimental manner.

The timing of DEX injections in this model was suggested by the observation that the stress of moving birds at 5 wk of age from brooder to growout houses appeared to be associated with increased incidence of colisepticemia in our initial field study. We thought TOC may later develop in a population of birds that survived the infection but were unable to completely kill the bacteria due to stress-induced immunosuppression. Later hormonal, social, environmental, and disease stresses during adolescence may then reactivate these sequestered infections resulting in TOC lesions. Recent studies have shown that this scenario may not be entirely the case. A second series of DEX injections produces a much higher incidence of TOC lesions (70 to 80%); however, *S. aureus* is isolated from most of these lesions both with and without *E. coli* challenge (Huff et al., 1999b). Surprisingly, air sac inoculation with *E. coli* is not necessary when multiple DEX treatments are used. In fact, TOC incidence is higher in birds not challenged, because there is less mortality before TOC lesions can develop. This result suggests that hatchery environmentally acquired opportunistic bacteria are also involved in our model.

This research suggests that there may be a cumulative effect of various stressors throughout turkey production

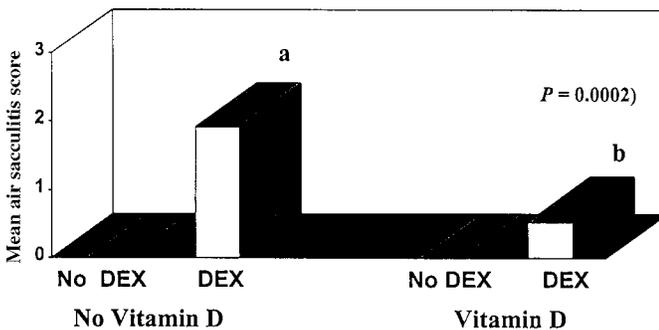


FIGURE 2. The effect of vitamin D₃ supplementation on air sacculitis scores of 14-wk-old male turkeys treated with dexamethasone (DEX) at 5 wk and again at 12 wk of age. ^{a,b}Superscripts denote a significant difference (*P* = 0.0002) due to vitamin D₃ supplementation of DEX-treated birds.

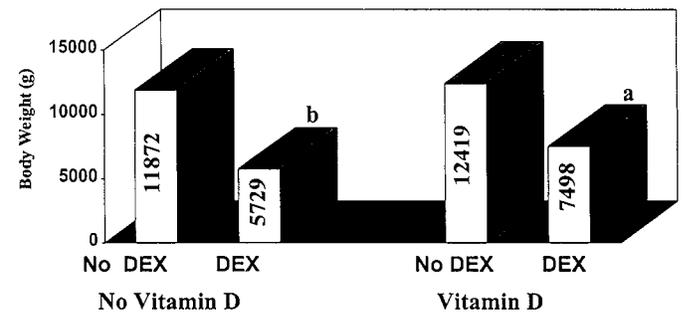


FIGURE 4. The effect of vitamin D₃ supplementation on mean body weight of 14-wk-old male turkeys that were treated with dexamethasone (DEX) at 5 wk and again at 12 wk of age. ^{a,b}Superscripts denote a significant difference (*P* = 0.0005) due to vitamin D₃ supplementation of DEX-treated birds.

that results in decreased resistance to bacterial infection. In all of the DEX studies, some individuals appear relatively unaffected by DEX treatment, whereas others succumb to respiratory disease and never recover. We believe this difference may be related to individual modulation of the stress response and the effect that response has on the immune system.

Vitamin D treatment significantly decreased TOC incidence in birds after a second series of DEX injections. The ability of vitamin D₃ supplementation to affect changes in the physiology and disease resistance of stressed birds emphasizes the current conceptual view that vitamin D₃ is a prohormone that affects all vital systems (DeLuca and Zierold, 1998) and that supplementation during stressful periods may help to modulate the immune response and increase resistance to opportunistic infection.

Vitamin D has long been known to be essential for calcium metabolism and is extremely important in bone physiology. However, understanding of the broad nature of this vitamin's activities has grown dramatically since the recognition of the seeming ubiquity of the vitamin D receptor (VDR). The VDR occurs not only in cells of the bone, kidney, liver, and intestine but also in tissues as diverse as the brain, heart, pancreas, parathyroid, bone marrow, stomach, and skin, as well as many of the organs and cells comprising the immune system (Stumpf, 1988; DeLuca, 1992; DeLuca and Zierold, 1998; Strugnell and DeLuca, 1998). These ubiquitous receptors are thought to mediate diverse regulatory activities through a single ligand, 1,25 (OH)₂ D₃ (Issa et al., 1998; Jones et al., 1998). The study of genetic differences in the sequence of the VDR was initiated by the discovery that these receptors regulate bone density (Morrison et al., 1994). These same genetic differences have also been shown to affect susceptibility to a number of infectious diseases in humans (Hill, 1998), and this may be related to the etiology of TOC. Vitamin D receptor polymorphisms have also been found to be associated with gender-related differences in growth rate in humans (Suarez et al., 1997, 1998). It seems possible that genetic selection for increased growth rate of turkeys, and concomitant immune changes, may involve the vitamin D receptor.

Chicks selected for a high level of TD have abnormal vitamin D metabolism (Xu et al., 1997; Mitchell et al., 1997), which has been inconsistently related to the number of intestinal and growth plate vitamin D receptors (Soares et al., 1990; Mitchell et al., 1997). Turkey osteomyelitis complex has been often, but inconclusively, associated with TD (Nairn, 1973; Wyers et al., 1991; Rath et al., 1994); however, the incidence of TD is usually much higher. Although the TD lesion itself may physically facilitate bacterial infection, the association between TD and TOC may also be due to the wide-ranging physiological effects of vitamin D metabolism and the commonality of dietary factors, environmental stressors, and genetics within any group of turkeys. Differences in VDR phenotypes rather than the numbers of these receptors may affect the incidence of both diseases, whereas the birds

that develop TOC may reflect a subgroup with an abnormally high stress response.

We have demonstrated that vitamin D supplementation of DEX-treated turkeys increased disease resistance and prevented or decreased DEX-induced changes in BW, relative organ weights, differential cell counts, and serum chemistries. The ability of supplemental vitamin D₃ to affect changes in the physiology and disease resistance of stressed birds emphasizes the current conceptual view that vitamin D₃ is a prohormone that is involved in homeostasis of all vital systems and that individual variation in the ability to metabolize or bind its metabolites may affect health and disease resistance in turkeys. It also suggests that selection based on VDR phenotype may be of value in the improvement of disease resistance and bone health in poultry stocks.

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