Evidence of Increased Cholecalciferol Requirement in Chicks with Tibial Dyschondroplasia

TIANSHUN XU,* ROLAND M. LEACH, JR.,² BRUCE HOLLIS,³ and JOSEPH H. SOARES, JR.*

*Nutritional Sciences Graduate Program and Department of Animal Sciences, University of Maryland, College Park, Maryland 20742, ‡Department of Poultry Science, Pennsylvania State University, University Park, Pennsylvania 16802, and ‡Department of Pediatrics, Medical University of South Carolina, Charleston, South Carolina 29425

ABSTRACT A series of experiments was conducted to test the hypothesis that vitamin D utilization may not be as efficient in chicks with tibial dyschondroplasia (TD). The basal diet contained 1.0% Ca and 0.45% available P with no supplemental cholecalciferol (D₃). Chicks from low TD (LTD) and high TD (HTD) selected lines were fed diets supplemented with various levels of vitamin D compounds and examined for rickets and TD. When chicks were fed a D₃-deficient diet containing only 1.25 mg/kg added D₃, HTD chicks had a greater incidence of severe rickets than LTD chicks (P < 0.05). The LTD chicks did not exhibit TD when fed a diet containing adequate (20 μg/kg) D₃. The LTD chicks fed a diet supplemented with 5 μg/kg D₃, however, had 22% incidence of TD. When HTD chicks were fed diets supplemented with 5 μg/kg D₃, the incidence of TD was highest. When HTD chicks were fed diets supplemented with 5 μg/kg D₃, further reduction of TD incidence (P < 0.05) occurred. A potentially toxic level of 1,25-(OH)₂D₃ (15 μg/kg) fed to HTD chicks resulted in still greater suppression of incidence of TD even though growth and feed intake in HTD chicks was greater than those of LTD chicks. It is concluded that the development of TD in HTD chicks is associated with subnormal ability to metabolize vitamin D.

(Key words: tibial dyschondroplasia, cholecalciferol metabolites, chick)

1997 Poultry Science 76:47-53

INTRODUCTION

Tibial dyschondroplasia (TD) is a skeletal disorder prevalent in commercial flocks of broilers and turkeys. It is characterized by an avascular plug of abnormal cartilage in the proximal metaphysis of the tibiotarsus and tarsalmetatarsus (Leach and Nesheim, 1965). This disorder occurs spontaneously and is similar to a generalized cartilage defect called osteochondrosis, which occurs in rapidly growing domestic animals such as swine (Reiland, 1978) and horses (Rejno and Stromberg, 1978).

Evidence of a genetic component in the etiology of TD has been provided by Leach and Nesheim (1965), Riddell (1976), and Sheridan et al. (1978). Although the precise cause of the disease is still unknown, several factors, such as copper deficiency (Leach and Nesheim, 1965), dietary tetraethylthiuram disulfide (Vargas et al., 1983; Veltmann et al., 1985), fusarochromanone (Walser et al., 1988; Wu et al., 1993), and elevated dietary chloride (Leach and Nesheim, 1965; Riddell, 1975a,b) will induce a high incidence of TD. Chickens fed diets with low calcium and high phosphorus had a high incidence of TD. Increasing dietary calcium can reduce the incidence of TD when chickens are fed diets high in phosphorus (Edwards and Veltmann, 1983). It was suggested that the effect of chloride on TD incidence is mediated through changes in acid-base balance. Sauveur et al. (1977) demonstrated that chickens made acidotic by consuming ammonium chloride showed reduced conversion of 25-hydroxycholecalciferol [25-(OH)D₃] to 1,25-dihydroxycholecalciferol [1,25-(OH)₂D₃] to 1,25-dihydroxycholecalciferol [1,25-(OH)₂D₃]. They suggested that abnormal vitamin D metabolism may be involved in TD. Using a diet low in calcium and high in phosphorus and chloride, Edwards (1989) demonstrated that dietary supplementation of D₃ and 25-(OH)D₃ alone reduced TD incidence. He suggested that TD is a conditioned manifestation of vitamin D deficiency in fast-growing broiler chicks. A recent report by Rennie et al. (1993) also indicated that supplemental dietary 1,25-(OH)₂D₃ reduced TD incidence in chickens fed a diet imbalanced in calcium and phosphorus.

In light of the association of a genetic predisposition for the development of TD and the apparent effective-
ness of vitamin D metabolite supplementation in reducing the incidence of TD (Edwards, 1989; Rennie et al., 1993), we hypothesized that the genetic predisposition may be related to an abnormality of the vitamin D endocrine system. Furthermore, previous observations suggested that chicks with TD possessed fewer vitamin D receptors than normal chicks (Soares et al., 1990). The objective of the present study was to investigate the relationship between the genetic predisposition for TD and vitamin D metabolism in the development of TD by comparing the response to dietary vitamin D steroids between broiler chicks from a line with low TD (LTD) incidence and a line with high TD (HTD) incidence. Both breeder lines were maintained at the Pennsylvania State University.

**MATERIALS AND METHODS**

**Animal and Diets**

Broiler chicks from the Pennsylvania State University LTD and HTD lines were hatched at the University of Maryland and used in the present studies. All experiments were conducted in electrically heated Petersime battery brooders with wire mesh floors in a windowless room in which continuous fluorescent lighting in the ceilings was shielded from chicks by the presence of sheet metal tops on the battery cages. The battery cages were each fitted with a 15 amp incandescent light bulb. The brooders were positioned in such a way as to minimize the variations in light density among different brooders and avoid direct exposure to the fluorescent light. Chicks were transferred to unheated growout battery cages at 21 d of age. Birds consumed feed and water *ad libitum*. The basal diet used in these studies is shown in Table 1. The basal diet contained 1.0% calcium and 0.45% available phosphorus. The basal diet was deficient in vitamin D3. All of the experiments employed a completely randomized design.

In Experiment 1, 90 newly hatched birds from each line were randomly divided to pens of 10 chicks each or a total of 30 birds per treatment. The design was a 2 × 3 × 3 factorial arrangement testing two lines of chicks and three D3 metabolites with three replications each. One treatment of birds was fed the basal diet with no supplemental D3, and the other two treatments were fed the basal diet supplemented with either inadequate D3 (1.25 μg/kg diet) or a slight excess of D3 (20 μg/kg diet). At the end of the experiment (25 d), all chicks were killed by cervical dislocation and examined for rickets and TD by making a longitudinal cut across the proximal tibia and scored for width of growth plate cartilage and hypertrophic chondrocytes (1 = normal, 4 = severe abnormal) (Edwards and Veltmann, 1983).

In Experiment 2, chicks from both lines were fed a diet containing adequate vitamin D3 (5 μg/kg diet) for the first 7 d. Then chicks from each line were randomly divided into six pens of six birds each. Three pens of chicks were fed a diet low in vitamin D3 (1.88 μg/kg of diet) and the other pens were fed a diet containing 5 μg D3/kg (adequate D3-NRC 1994) of diet until Day 30 when the chicks were killed and scored for rickets and TD.

In Experiment 3, 120 day-old chicks from the HTD line were randomly divided into 12 pens of 10 birds each. Each of the four dietary treatments were randomly assigned to three pens of chicks. The dietary treatments were as follows: 5 (control) or 20 μg D3, 5 μg 1,25-(OH)2D3 (kindly provided by M. Uskokovic) or a combination of 20 μg D3 plus 5 μg 1,25-(OH)2D3/kg of diet, respectively. At 4 wk of age, blood samples were taken from six birds per treatment to determine serum calcium and 1,25-(OH)2D3. All chicks were weighed and then killed as before, examined for TD and scored for its severity.

In Experiment 4, day-old chicks from the HTD line were randomly divided into 12 pens of 10 birds each. Each of the three dietary treatments were randomly assigned to three pens of chicks. The dietary treatments were as follows: 5 (control) or 20 μg D3, 5 μg 1,25-(OH)2D3 (kindly provided by M. Uskokovic) or a combination of 20 μg D3 plus 5 μg 1,25-(OH)2D3/kg of diet, respectively. At 4 wk of feeding, blood samples were taken from both asymptomatic and symptomatic (TD) chicks from all pens and analyzed for serum calcium. All chicks were weighed and then killed (as above), examined for TD and scored for its severity. Left tibias were taken from both asymptomatic and symptomatic chicks from all pens for bone ash determination.

In Experiment 5, day-old chicks from the LTD line and the HTD line were divided into six pens of six birds each. The treatment groups were: control (20 μg D3/kg diet) and 1,25-(OH)2D3 (15 μg/kg) such that the design was a 2 × 2 × 3 factorial with two lines of chicks by two D3 metabolites by three replications. Each replication contained six pens of six birds each. At 4 wk of feeding, blood samples were taken from both asymptomatic and symptomatic (TD) chicks from all pens and analyzed for serum calcium. All chicks were weighed and then killed (as above), examined for TD and scored for its severity.
the width of rachitic growth plate. As dietary vitamin D levels increased, severe rickets incidence was decreased significantly. There were also a significant interaction between dietary vitamin D levels and chick strains in severe rickets incidence (P < 0.05). The incidence of severe rickets was higher in HTD chicks than in LTD chicks when chicks were fed a diet supplemented with 1.25 μg D3/kg of diet. There were very significant (P < 0.01) effects on TD incidence by chick strain, dietary vitamin D level, and by an interaction between strain and vitamin D level. About 27% of chicks from the HTD line developed TD when fed a diet supplemented with 20 μg D3/kg, whereas no incidence of TD was observed for the LTD chicks.

The results from Experiment 2 show that there were no differences in the incidence of rickets (Table 3) between either line of chicks receiving a low vitamin D3 diet (1.88 μg or 75 IU D3/kg). Supplementation of the basal diet with 5 μg or 200 IU D3/kg, the recommended requirement as established by the NRC (1994), prevented the development of rickets in both lines of chicks. There was no effect on rickets incidence by chick strains. No interaction in rickets incidence was found between strains and vitamin D levels. As dietary vitamin D levels increased, rickets incidence was reduced significantly (P < 0.01). Incidence of TD was affected by chick strain and vitamin D levels. The HTD chicks had a greater TD incidence than LTD chicks. As dietary vitamin D level was increased from 1.88 to 5 μg/kg of diet, TD incidence increased, whereas rickets incidence decreased to zero. This result indicates that rickets may mask TD at low vitamin D levels. Chicks from the LTD line did not develop TD when fed the low vitamin D diet. However, when fed a diet with 5 μg D3/kg, a significantly higher (22%) incidence of TD occurred in LTD chicks. The incidences of TD were greater in HTD chicks than in the LTD chicks fed either the sufficient (5 μg/kg) or low D3 (1.88 μg/kg) diets.

### RESULTS

In Experiment 1 (Table 2), there were no differences in the incidence of rickets between the LTD and HTD lines of chicks when they were fed diets deficient in vitamin D3 (0 or 1.25 μg D3/kg diet). There were also no significant interactions between dietary vitamin D levels and strains. However, as compared to LTD chicks, HTD chicks had a significantly higher incidence (39 ± 2.8 vs 25 ± 2.8) of severe rickets, which was determined by the width of rachitic growth plate. As dietary vitamin D levels increased, severe rickets incidence was decreased significantly. There were also a significant interaction between dietary vitamin D levels and chick strains in severe rickets incidence (P < 0.05). The incidence of severe rickets was higher in HTD chicks than in LTD chicks when chicks were fed a diet supplemented with 1.25 μg D3/kg of diet. There were very significant (P < 0.01) effects on TD incidence by chick strain, dietary vitamin D level, and by an interaction between strain and vitamin D level. About 27% of chicks from the HTD line developed TD when fed a diet supplemented with 20 μg D3/kg, whereas no incidence of TD was observed for the LTD chicks.

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### TABLE 2. Effect of different levels of cholecalciferol (D3) on the incidence of rickets in chicks from LTD and HTD lines

<table>
<thead>
<tr>
<th>Chick line</th>
<th>Dietary vitamin D3 (μg/kg)</th>
<th>Rickets (%)</th>
<th>Severe rickets (%)</th>
<th>TD (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LTD</td>
<td>0</td>
<td>100</td>
<td>43 ± 6.7</td>
<td>0</td>
</tr>
<tr>
<td>HTD</td>
<td>0</td>
<td>100</td>
<td>54 ± 6.7</td>
<td>0</td>
</tr>
<tr>
<td>LTD</td>
<td>1.25</td>
<td>96 ± 3.6</td>
<td>33 ± 6.4</td>
<td>0</td>
</tr>
<tr>
<td>HTD</td>
<td>1.25</td>
<td>100</td>
<td>63 ± 3.3</td>
<td>0</td>
</tr>
<tr>
<td>LTD</td>
<td>20</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>HTD</td>
<td>20</td>
<td>0</td>
<td>0</td>
<td>27 ± 12</td>
</tr>
</tbody>
</table>

*Means in a column with no common superscript differ significantly (P < 0.05).

1LTD, HTD; low and high incidence, respectively, of tibial dyschondroplasia lines of broiler chicks obtained from Pennsylvania State University.

2Values are means ± pooled SEM, n = 3 for all measurements.

### Determination of Calcium and 1,25-(OH)2D3

Serum was diluted 50-fold with 5 g/L lanthanum oxide. Serum calcium was determined by atomic absorption spectrophotometry using a Perkin-Elmer Model 5100 PC.5 Serum 1,25-(OH)2D3 levels were determined by the method of Hollis (1986).

### Statistical Analysis

Analyses of variance was conducted using the General Linear Models procedure of SAS® (SAS Institute, 1988). Data expressed as percentages were log transformed prior to statistical analysis. For Experiments 1, 2, and 5 in which treatments were in a factorial arrangement, data were analyzed for main effects and interactions. The LSD tests were performed for multiple comparisons of means. Values given are means ± SEM and the α value was 5%.

### TABLE 3. Effect of different levels of cholecalciferol (vitamin D3) on the incidences of rickets and tibial dyschondroplasia (TD) in LTD and HTD line chicks, Experiment 2

<table>
<thead>
<tr>
<th>Chick line</th>
<th>Dietary cholecalciferol (μg/kg)</th>
<th>Rickets (%)</th>
<th>TD (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LTD</td>
<td>1.88</td>
<td>94 ± 5.6</td>
<td>0</td>
</tr>
<tr>
<td>HTD</td>
<td>1.88</td>
<td>89 ± 5.6</td>
<td>11 ± 5.6</td>
</tr>
<tr>
<td>LTD</td>
<td>5</td>
<td>0</td>
<td>22 ± 5.6</td>
</tr>
<tr>
<td>HTD</td>
<td>5</td>
<td>0</td>
<td>67±</td>
</tr>
</tbody>
</table>

*Means in a column with no common superscript differ significantly (P < 0.05).

1Means ± pooled SEM, n = 3 for all measurements. LTD = Low TD incidence; HTD = High TD incidence.
suggesting that 1,25-(OH)\textsubscript{2}D\textsubscript{3} treatment alone reduced compared to chicks receiving the control (5 gD\textsubscript{3}/kg) diet significantly reduced TD incidence in HTD chicks (Table 4) the serum 1,25-(OH)\textsubscript{2}D\textsubscript{3} levels in both LTD and groups. Previously, we had determined (unpublished significant differences (LTD 43 ± 0.8 vs HTD 39 ± 0.2 mg/dL). Addition of 20 µg D\textsubscript{3} or 5 µg 1,25-(OH)\textsubscript{2}D\textsubscript{3} alone did not alter serum calcium levels, but the combination of the two increased (P < 0.01) serum calcium level (Table 4).

In Experiment 5, the effects of adding slightly toxic doses of the active metabolite, i.e., 15 µg 1,25-(OH)\textsubscript{2}D\textsubscript{3}/kg, (Soares et al., 1983) were investigated. There were no significant differences between two strains in body weight gain and feed efficiency when fed the Control (20 µg D\textsubscript{3}/kg) diet. Addition of 15 µg 1,25-(OH)\textsubscript{2}D\textsubscript{3}/kg reduced weight gain and feed conversion in both lines of chicks (Table 6) compared to controls (P < 0.01). In addition, there were significant (P < 0.01) interactions between vitamin D and strains in terms of growth rate. The decrease in weight gain when fed high levels of 1,25-(OH)\textsubscript{2}D\textsubscript{3} were 32 and 14% for LTD and HTD line chicks, respectively. This indicates that HTD chicks may be more resistant to 1,25-(OH)\textsubscript{2}D\textsubscript{3} toxicity than LTD chicks. There were very significant (P < 0.01) main effects and interactions on TD incidence and severity by chick strains and vitamin D levels. Addition of 15 µg 1,25-(OH)\textsubscript{2}D\textsubscript{3} to diet of HTD chicks completely prevented the development of TD. There were differences in serum Ca levels between LTD chicks (9.0 ± 0.24) and HTD chicks (9.9 ± 0.24). Addition of high levels of 1,25-(OH)\textsubscript{2}D\textsubscript{3} increased serum Ca level (10.4 ± 0.23) as compared to control diet (9.3 ± 0.21). No interaction in serum Ca level was found between strains and vitamin D level.

### Table 4. Effect of different levels of cholecalciferol and 1,25-dehydroxycholecalciferol [1,25-(OH)\textsubscript{2}D\textsubscript{3}] on the incidence of tibial dyschondroplasia (TD) and serum Ca and 1,25-(OH)\textsubscript{2}D\textsubscript{3} levels in chicks from HTD line, Experiment 3\textsuperscript{1}

<table>
<thead>
<tr>
<th>Dietary treatment</th>
<th>Body weight</th>
<th>Incidence (1\textsuperscript{2})</th>
<th>Severity score (2\textsuperscript{2})</th>
<th>1,25-(OH)\textsubscript{2}D\textsubscript{3}</th>
<th>Ca (1\textsuperscript{2})</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 µg D\textsubscript{3}</td>
<td>619 ± 6</td>
<td>97 ± 3.3\textsuperscript{a}</td>
<td>2.2 ± 0.1&lt;sup&gt;2&lt;/sup&gt;</td>
<td>35 ± 4.9</td>
<td>9.2 ± 0.2&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>20 µg D\textsubscript{3}</td>
<td>587 ± 23</td>
<td>57 ± 6.7&lt;sup&gt;b&lt;/sup&gt;</td>
<td>2.3 ± 0.1</td>
<td>32 ± 0.2</td>
<td>9.8 ± 0.16&lt;sup&gt;ab&lt;/sup&gt;</td>
</tr>
<tr>
<td>5 µg 1,25-(OH)\textsubscript{2}D\textsubscript{3}</td>
<td>598 ± 21</td>
<td>40 ± 0&lt;sup&gt;b&lt;/sup&gt;</td>
<td>2.3 ± 0.2</td>
<td>28 ± 4.5</td>
<td>9.2 ± 0.24&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>20 µg D\textsubscript{3} and 5 µg 1,25-(OH)\textsubscript{2}D\textsubscript{3}</td>
<td>598 ± 25</td>
<td>33 ± 17.6&lt;sup&gt;b&lt;/sup&gt;</td>
<td>1.6 ± 0.8</td>
<td>39 ± 3.5</td>
<td>10.2 ± 0.20&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

\textsuperscript{a,b}Values in a column with no common superscript differ significantly (P < 0.05).

\textsuperscript{1}Values are means ± SEM, n = 3 for all measurements except serum calcium (n = 6).

\textsuperscript{2}Severity score 1 to 4 with 4 most severe for TD.

### Table 5. Effect of 1,25-dihydroxycholecalciferol [1,25-(OH)\textsubscript{2}D\textsubscript{3}] on growth, bone ash, the incidence and severity of tibial dyschondroplasia (TD), and serum Ca levels in a line of chicks with a high incidence of TD, Experiment 4\textsuperscript{1}

<table>
<thead>
<tr>
<th>Dietary D\textsubscript{3} metabolite</th>
<th>Body weight</th>
<th>Incidence</th>
<th>Severity (2\textsuperscript{2})</th>
<th>Asymptomatic chicks (7)</th>
<th>Symptomatic chicks (6)</th>
<th>Asymptomatic chicks (9)</th>
<th>Symptomatic chicks (6)</th>
<th>Bone ash</th>
<th>Serum Ca</th>
</tr>
</thead>
<tbody>
<tr>
<td>20 µg D\textsubscript{3}</td>
<td>606 ± 14</td>
<td>83 ± 9.6&lt;sup&gt;a&lt;/sup&gt;</td>
<td>2.6 ± 0.1</td>
<td>45 ± 0.8&lt;sup&gt;b&lt;/sup&gt;</td>
<td>48 ± 1.1</td>
<td>10.9 ± 0.2</td>
<td>10.1 ± 0.2&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10 µg 1,25-(OH)\textsubscript{2}D\textsubscript{3}</td>
<td>611 ± 43</td>
<td>33 ± 9.6&lt;sup&gt;b&lt;/sup&gt;</td>
<td>2.9 ± 0.1</td>
<td>48 ± 1.2&lt;sup&gt;a&lt;/sup&gt;</td>
<td>48 ± 1.2</td>
<td>10.9 ± 0.2</td>
<td>10.1 ± 0.2&lt;sup&gt;b&lt;/sup&gt;</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\textsuperscript{a,b}Values within a column with no common superscript differ significantly (P < 0.05).

\textsuperscript{1}Values are means ± SEM, n = 3 for body weight, TD incidence, and severity. The number of chicks assayed for bone ash and serum Ca is listed in parentheses.

\textsuperscript{2}Severity = Scale is 1 to 4 with 4 most severe TD.

\textsuperscript{3}Indicates samples unavailable for assay (only one asymptomatic chick).
1,25-(OH)2D3, LTD line chicks exhibited significantly fed a diet supplemented with potentially toxic levels of required to prevent TD formation in HTD chicks. When High levels (15 Sorensen, 1987), the effect of 1,25-(OH)2D3 on TD growth rate is associated with decreased TD incidence rate was also decreased (Thorp diet reduced TD incidence in a high TD line, but growth completely prevented by adequate vitamin D3 sup-

TD incidence in broiler chicks selected for a high (TD genetic line HTD 15 m LTD 15 m HTD Control 2 484 563 100 ± 19a 100 ± 4.2a 1.67 ± 0.04a 41 ± 10a 2.3 ± 0.2a 9.3 ± 0.26b 12c b 0b 0b 10.4 ± 0.54a

**DISCUSSION**

The present studies have demonstrated that dietary supplementation with D3 or 1,25-(OH)2D3 can decrease TD incidence in broiler chicks selected for a high incidence of TD. The development of TD could be completely prevented by adequate vitamin D3 sup-

**TABLE 6. Effect of 1,25-dihydroxycholecalciferol [1,25-(OH)2D3] and 1-α-hydroxycholecalciferol [1-α(OH)D3] on performance and incidence and severity of tibial dyschondroplasia (TD) in a high (HTD) and low (LTD) TD line of chicks, Experiment 5**

<table>
<thead>
<tr>
<th>Genetic line</th>
<th>Dietary treatment</th>
<th>4-wk gain</th>
<th>Feed:gain</th>
<th>TD</th>
</tr>
</thead>
<tbody>
<tr>
<td>LTD</td>
<td>Control</td>
<td>563 ± 11a</td>
<td>100 ± 19a</td>
<td>1.65 ± 0.02b 0b 0b 8.6 ± 0.24b</td>
</tr>
<tr>
<td>HTD</td>
<td>Control</td>
<td>484 ± 21b</td>
<td>100 ± 4.2a</td>
<td>1.67 ± 0.04a 41 ± 10a 2.3 ± 0.2a 9.3 ± 0.26b</td>
</tr>
<tr>
<td>LTD</td>
<td>15 μg 1,25-(OH)2D3</td>
<td>381 ± 19d</td>
<td>68 ± 3.4b</td>
<td>1.81 ± 0.04a 0b 0b 9.3 ± 0.27b</td>
</tr>
<tr>
<td>HTD</td>
<td>15 μg 1,25-(OH)2D3</td>
<td>444 ± 12c</td>
<td>86 ± 2.4c</td>
<td>1.78 ± 0.02a 0b 0b 10.4 ± 0.54a</td>
</tr>
</tbody>
</table>

a–dValues in a column with no common superscript differ significantly (P < 0.05).

1Means ± SEM, n = 3 for all measurements except serum Ca (n = 6).

2The basal diet was supplemented with 20 μg D3/kg.

3Severity score 1 to 4 with 4 most severe.

**TABLE 6. Effect of 1,25-dihydroxycholecalciferol [1,25-(OH)2D3] and 1-α-hydroxycholecalciferol [1-α(OH)D3] on performance and incidence and severity of tibial dyschondroplasia (TD) in a high (HTD) and low (LTD) TD line of chicks, Experiment 5**

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1Means ± SEM, n = 3 for all measurements except serum Ca (n = 6).

2The basal diet was supplemented with 20 μg D3/kg.

3Severity score 1 to 4 with 4 most severe.

studies, we were able to decrease TD incidence by increasing dietary vitamin D3 levels or by supplementa-

dietary vitamin D, although changes in TD incidence and serum calcium were noted. A similar observation has been made by others (Rennie et al., 1993). It has also been reported that plasma 1,25-(OH)2D3 levels were relatively unchanged even in vitamin D intoxication (Sheppard and Deluca, 1980).

Furthermore, it is known that all of the major vitamin D metabolites are primarily bound to plasma vitamin D binding protein (DBP) and secondarily to albumin. The affinity of DBP for 1,25-(OH)2D3 is low compared to most of the other vitamin D metabolites (Haddad, 1987). Therefore, the free or unbound fraction of 1,25-(OH)2D3 in circulation should increase more than with other vitamin D metabolites as the occupancy of DBP with D3 metabolites with higher affinity increases. Dietary sup-

increase in the proportion of free 1,25-(OH)2D3. A
number of studies have shown that the delivery of sterols to tissues and cells was restricted by their association with extracellular DBP (Manolalgas and Deftos, 1980; Adams, 1984; Ron et al., 1984; Haddad et al., 1988). Additionally, recent reports have demonstrated that cellular responses to D3 metabolites were correlated with free concentrations of 1,25-(OH)2D3 (Vanham et al., 1988; Bikle and Gee, 1989). Thus, it is possible that serum levels of free 1,25-(OH)2D3 are increased even though the concentrations of total 1,25-(OH)2D3 were not changed in our studies and the increased free 1,25-(OH)2D3 effected the reduction in TD incidence. This point needs further investigation.

It has been previously shown that dietary supplementation with 1,25-(OH)2D3 can decrease TD incidence (Edwards, 1989, 1990; Rennie et al., 1993). In these studies, diets were low in calcium, high in phosphorus and chlorine, or imbalanced in calcium and phosphorus, and it is possible that the effects of feeding vitamin D3 metabolites on TD incidence was likely through increasing calcium absorption. In the present studies, the basal diet used contained an adequate amount of calcium and lower but adequate P levels. We also employed the Pennsylvania State University line predisposed to TD. The results obtained indicate that supplementation of vitamin D metabolites [1,25-(OH)2D3] can prevent development of TD in genetically predisposed chicks. As there were no differences in serum calcium and bone ash between TD and asymptomatic HTD chicks fed a diet sufficient in D3, the effects of 1,25-(OH)2D3 on TD development is likely due to a more direct effect on growth plate chondrogenesis. Recent studies have demonstrated 1,25-(OH)2D3 is a potent regulator of cell proliferation and differentiation and may play important roles in cell maturation (Walters, 1992). It has also been reported that 1,25-(OH)2D3 promotes chondrocyte maturation (Gerstenfeld, 1988, 1990). The chondrocytes in TD-associated growth plate remain hypertrophic and fail to reach complete maturation (Hargest et al., 1985). Because our studies showed that higher dietary concentrations of 1,25-(OH)2D3 were required to prevent TD in HTD chicks it may be that chondrocytes of TD chicks require higher titers of 1,25-(OH)2D3 to effect cell maturation. The specific defect of TD will require further studies.

**REFERENCES**


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