Susceptibility of 4 commercial broiler crosses to lameness attributable to bacterial chondronecrosis with osteomyelitis

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ABSTRACT Growing broilers on wire flooring provides an excellent experimental model for exposing susceptibility to lameness attributable to bacterial chondronecrosis with osteomyelitis (BCO). Two independent experiments (E1, E2) were designed to compare the susceptibilities of broilers from 4 commercial crosses (W, X, Y, and Z). The standard crosses (W and Y) grow rapidly at an early age, whereas high-yield crosses (X and Z) initially tend to grow more slowly. Chicks were obtained from a commercial hatchery for E1, or were hatched at the University of Arkansas Poultry Research Hatchery for E2. Males and females were reared together (E1; n = 360/cross) or separately (E2; n = 390/cross) in 3 × 3 m pens on litter or wire flooring (wire). Necropsies revealed lesions that were pathognomonic for BCO in ≥94% of the birds that became lame. The SigmaStat Z-test was used to compare cumulative lameness incidences at 8 wk of age. For birds reared on litter, lameness incidences were low and did not differ between crosses or sexes (range: 2.2 to 4.6%; $P \geq 0.6$). When males were reared on wire, their lameness incidences (by cross) were E1 = 52% for W^b; 42% for X^c; 69% for Y^a, and 44% for Z^{bc}; E2 = 31% for W^b; 19% for X^c; 49% for Y^a; and 25% for Z^{bc}. For females reared on wire, the lameness incidences were E1 = 40% for W^b, 30% for X^c, 49% for Y^a, and 28% for Z^c; E2 = 16% for W; 15% for X; 16% for Y; and 15% for Z (ns). Accordingly, the hierarchical ranking for BCO susceptibility by broiler cross was X ≤ Z ≤ W < Y for males in E1 and E2, for females in E1, and for males and females pooled in E1 and E2. Standard broiler crosses developed higher incidences of lameness than high-yield crosses, implicating an association between rapid early growth and susceptibility to BCO. Rearing the females separately on wire in E2 led to uniformly low incidences of BCO, regardless of cross. Stress-mediated immunosuppression contributes to the pathogenesis of BCO; perhaps female broilers experience less social or competitive stress when reared separately from their male hatch mates.

Key words: lameness, broiler, osteomyelitis, bone, growth

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INTRODUCTION

Bacterial chondronecrosis with osteomyelitis (**BCO**) is considered the most common cause of lameness in commercial broilers worldwide (Pattison, 1992; McNamee et al., 1998; Butterworth, 1999; McNamee and Smyth, 2000; Bradshaw et al., 2002; Dinev, 2009). This category of lameness previously was known as femoral head necrosis (FHN) but recently has been relabeled BCO (McNamee and Smyth, 2000) in recognition that necrosis and infection occur not only within the proximal head of the femur, but also in other bones that are subjected to severe torque and shear stress such as the proximal tibiotarsus (hereafter referred to as the tibia) and the fourth thoracic (**T4**) vertebra (e.g., spondylopathy or spondylitis). The T4 vertebrae articulate between the fused vertebrae of the notarium cranially and the bony pelvis caudally. The pathogenesis leading to BCO is believed to be initiated by mechanical damage (e.g., osteochondrosis) to poorly aligned and structurally unstable columns of chondrocytes (cartilage cells) in the growth plates, followed by colonization of osteochondrotic clefts by hematogenously distributed opportunistic bacteria (Carnagan, 1966; Wise, 1971; Nairn and Watson, 1972; McCaskey et al., 1982; Riddell et al., 1983; Duff, 1984, 1989a,b; Emslie et al., 1984; Griffiths et al., 1984; Duff and Randall, 1987; Thorp and Duff, 1988; Hocking, 1992; Riddell, 1992; Tate et al., 1993; Thorp et al., 1993; Thorp, 1994; Thorp and Waddington, 1997; McNamee and Smyth, 2000; Joiner et al., 2005; Wideman and Prisby, 2013). Bacteria transmitted to chicks from breeder parents, contaminated eggshells, or hatchery sources (Skeeles, 1997; McCullagh et al.,

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1998; Rodgers et al., 1999; McNamee and Smyth, 2000; Stalker et al. 2010; Kense and Landman, 2011), or that enter the chick's circulation via translocation through the integument, respiratory system, or gastrointestinal tract (Mutalib et al., 1983a,b; Andreasen et al., 1993; Thorp et al., 1993; McNamee et al., 1999) spread hematogenously and exit the bloodstream through the fenestrated endothelium of capillaries supplying the growth plate (Beaumont, 1967; Lutfi, 1970b; Hunt et al., 1979; Howlett, 1980; Howlett et al., 1984; Emslie and Nade, 1983, 1985).

It has been difficult to investigate the etiology, pathogenesis, and treatment strategies for BCO because spontaneous incidences typically are highly variable and occur only sporadically in research flocks. Experimental models for consistently triggering BCO are needed to systematically evaluate prophylactic and therapeutic treatments. Attempts to initiate BCO via respiratory challenges with pathogenic bacteria have been marginally successful (Devriese et al., 1972; Mutalib et al., 1983b; Jensen et al., 1987; Nicoll and Jensen, 1987; McNamee et al., 1999), whereas BCO has repeatedly been reproduced by injecting broilers and turkeys intravenously with appropriate strains of *Staphylococcus* spp. (Carnaghan, 1966; Wise, 1971; Nairn, 1973; Emslie and Nade, 1983, 1985; Emslie et al., 1983; Kibenge et al., 1983; Mutalib et al., 1983a; Griffiths et al., 1984; Alderson et al., 1986; Daum et al., 1990). Recently we developed a wire flooring model for reliably triggering high incidences of BCO without purposefully exposing broilers to known pathogens (Wideman et al., 2012). [Provisional patent No. 61/499,954 protects the exclusive rights of the University of Arkansas to all uses of the wire flooring technology within the context of evaluating or developing treatments for inducing lameness attributable to osteochondrosis, chondronecrosis, and osteomyelitis in poultry.] It is our hypothesis that the sustained footing instability induced by wire flooring exposes susceptible joints to persistent additional torque and shear stress. Presumably the resulting micro-trauma, osteochondrosis, and vascular obstruction within the epiphyseal-physeal cartilage initiates focal necrosis and bacterial colonization by blood-borne bacteria (Wideman and Prisby, 2013). The successful use of probiotics to substantially reduce the incidence of BCO on wire flooring implicates the gastrointestinal tract as an important portal of entry for blood-borne bacteria (Wideman et al., 2012). Wire flooring per se also likely constitutes a significant stressor contributing to generalized immunosuppression and thus bacterial proliferation. For example, elevated flooring systems that deprive birds of access to litter stimulate chronic stress, including elevated blood corticosterone concentrations and immunosuppression (El-Lethey et al., 2003). Chronic stress and immunosuppression have been implicated in the etiology of spontaneous BCO outbreaks in commercial poultry flocks (Mutalib et al., 1983a,b; Andreasen et al., 1993; McNamee et al., 1998, 1999; Butterworth, 1999; Huff et al., 2000; McNamee and Smyth, 2000) and in the pathogenesis of turkey osteomyelitis complex (**TOC**; Wyers et al., 1991; Huff et al., 1998, 1999, 2000, 2005, 2006). Glucocorticoid injections have been used to experimentally simulate chronic stress and trigger TOC in turkeys (Huff et al., 1998, 1999), and femoral or tibial head necrosis in Leghorn hens and broilers (Cui et al., 1997; Durairaj et al., 2012; Wideman and Pevzner, 2012).

Genotype and selection for growth performance have been implicated in the susceptibility of broilers and turkeys to impaired walking ability (Wise, 1970a,b; Nestor, 1984; Kestin et al., 1992, 1999, 2001; Nestor and Anderson, 1998) as well as to a variety of leg disorders including tibial dyschondroplasia (Leach and Nesheim, 1972; Riddell, 1976; Sheridan et al., 1978; Walser et al., 1982; Zhang et al., 1995; Kuhlers and McDaniel, 1996), spondylolisthesis or kinky back (Riddell, 1973, 1976; Wise, 1973; Khan et al., 1977), valgus-varus deformities (Mercer and Hill, 1984; Sorensen, 1992), and twisted leg or perosis (Somes, 1969; Haye and Simons, 1978; Mercer and Hill, 1984; Sorensen, 1992). In some but not all comparisons, faster growing lines or crosses tend to exhibit higher incidences of leg disorders and impaired walking ability when compared with slower growing lines (Nestor, 1984; Sorensen, 1992; Kuhlers and McDaniel, 1996; Kestin et al., 1999, 2001). The highest incidences of leg weakness tend to occur in the fastest growing broiler flocks, and management strategies that reduce early growth rates tend to reduce the incidence of skeletal disorders and lameness (Riddell, 1983; Duff and Thorp, 1985; Robinson et al., 1992; Havenstein et al., 1994; Hester, 1994; McNamee et al., 1999; Su et al., 1999; Kestin et al., 2001; Bradshaw et al., 2002; Julian, 2005). These observations support a consensus hypothesis that the skeleton does not mature rapidly enough to support the dramatic maximum growth potential of modern broilers (Sorensen, 1992; Kestin et al., 2001). In the present study the wire flooring model enabled us to compare for the first time the potential impact of genotype on the susceptibility of commercial broilers to BCO. Four broiler crosses, designated W, X, Y, and Z, were evaluated in 2 experiments (E1 and E2). Crosses W and Y are standard crosses that grow rapidly at an early age, whereas X and Z are high-yield crosses that initially tend to grow more slowly. These crosses are commercially available to broiler integrators worldwide. All chicks were obtained from a commercial hatchery for E1, whereas in E2 the chicks were hatched at the University of Arkansas Poultry Research Farm.

MATERIALS AND METHODS

Animal procedures were approved by the University of Arkansas Institutional Animal Care and Use Committee (protocol 11002). Two independent experiments were conducted using 22 pens (E1) or 24 pens (E2) in building A364 East at the University of Arkansas Poultry Research Farm. Pens were 3 × 3 m with flooring consisting of clean wood shavings litter (n = 6 or

8 litter pens in E1 and E2, respectively) or raised wire panels (n = 16 wire pens in both experiments). The wire panels were constructed from 5 cm × 5 cm lumber and were 3 m long and 1.5 m wide, with 5 cm × 5 cm cross members added for support. Hardware cloth (1.3 cm × 2.54 cm mesh = 0.5 inch × 1 inch, 0.063-gauge, galvanized welded wire cloth; Direct Metals, Kennesaw, GA) was fastened to the top of the frame and cross-members. The panels were elevated on 30-cm-high masonry blocks to permit manure to pass through and accumulate underneath the wire surface. Tube feeders were positioned at the front, and nipple waterers were positioned at the rear of each pen, thereby forcing the chicks to traverse the length of the floor to eat and then drink. Between experiments the pens were disassembled and the wire flooring panels were cleaned using a pressure washer and detergent.

Chicks from crosses W, X, Y, and Z were obtained from a commercial hatchery on April 27, 2012, for E1. Fertile eggs for the same crosses were hatched and vent-sexed at the University of Arkansas Poultry Research Hatchery on September 7, 2012, for E2. The chicks were not vaccinated. Pen assignments by line and sex are shown in Figure 1. Females and males were reared together in E1. Twenty wing-banded chicks per cross were placed in each of the 6 litter pens, and bird density was reduced to 15 clinically healthy chicks per cross on d 14. Four wire pens were allocated to each cross, with each pen initially containing 80 chicks. On d 14, the bird density was culled to 60 clinically healthy chicks per pen. The sexes were reared separately in E2. Two litter pens and 4 wire pens were assigned per cross. Each pen initially contained 80 males or 80 females from the designated cross, and on d 14 all pens were culled to 65 of the largest chicks (Figure 1). The early culling protocol was instituted after necropsies of runts and culls during the first 2 wk revealed macroscopic evidence of systemic bacterial infection including osteomyelitis (Wideman et al., 2012). The photoperiod was set for 23L:1D. Thermoneutral temperatures were maintained throughout with target temperatures set at 32°C for d 1 to 3, 30°C for d 4 to 6, 28°C for d 7 to 10, 26°C for d 11 to 14, and 24°C thereafter. Feed and water were provided ad libitum. The starter diet was a commercial corn- and soybean-meal-based chick starter (crumbles), and after d 35 all birds were switched to a pelleted commercial corn- and soybean-meal-based finisher diet. Feed was formulated without meat or animal byproducts to meet or exceed minimum NRC (1994) standards for all ingredients.

Beginning on d 15, all birds were observed daily to detect the onset lameness. Lameness typically began after d 35 and progressed rapidly in birds that during the preceding 24 to 48 h appeared to be healthy. Affected broilers had difficulty standing, exhibited an obvious limping gait while dipping one or both wing tips and, if not removed, become completely immobilized within 3 d. Birds were removed as soon as the onset of lameness was noticed and were euthanized via CO_2 gas inhalation. As was indicated by Dinev (2009), lame birds with BCO can die quickly because they have difficulty accessing food and water. Therefore, birds found dead also were necropsied to ascertain the cause of death and assess leg lesions. Body weights were not recorded in E1, whereas all pens were weighed on d 35 and 56 in E2. Survivors on d 56 were considered to be clinically healthy and were not necropsied to assess subclini-

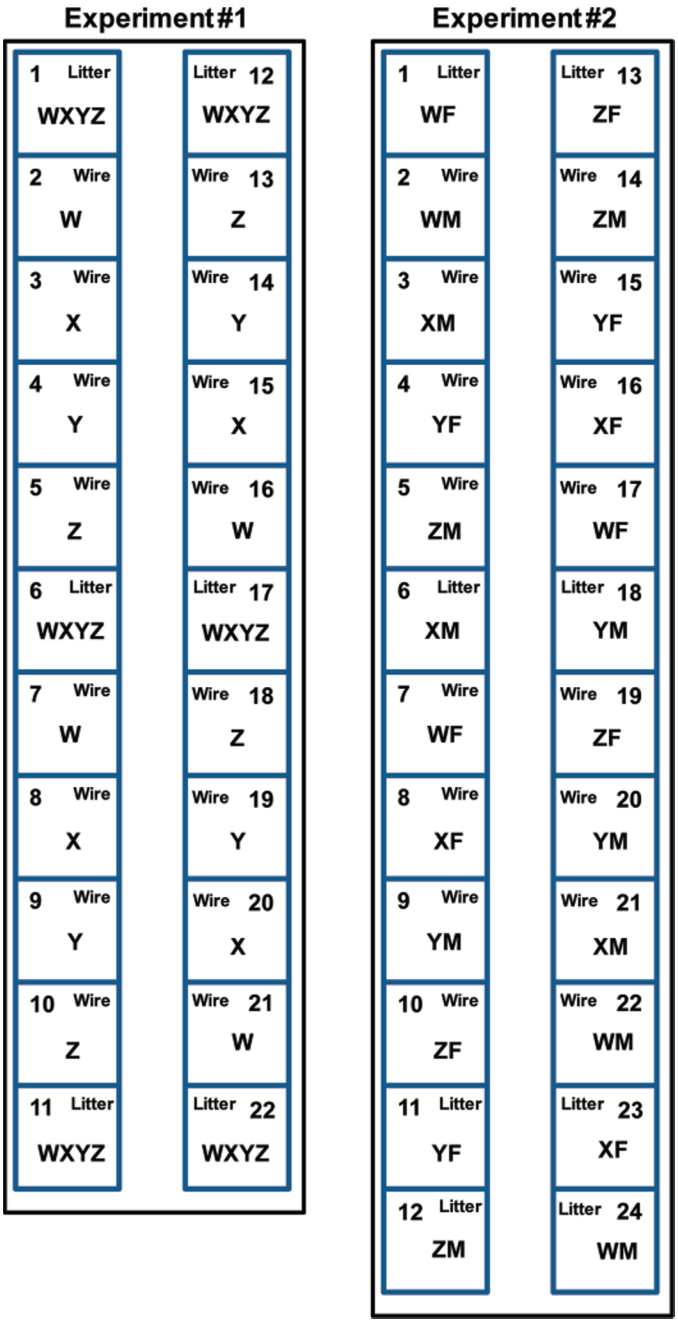

Figure 1. Arrangement of 22 pens in experiment 1 and 24 pens in experiment 2. The pens had either wood shavings litter (litter) or flat wire flooring (wire). In experiment 1, males and females were reared together, and on d 14 the 6 litter pens were culled to 15 clinically healthy wing banded chicks from each of 4 commercial broiler crosses (W, X, Y, and Z). The 18 wire pens contained 60 chicks (males and females together) reared separately by cross. In E2, the males (M) and females (F) of all crosses were reared separately, with 65 chicks per pen beginning on d 14. Color version available in the online PDF.

cal lesion incidences in either experiment. Euthanized birds were necropsied within 20 min postmortem. Each bird's sex was confirmed by necropsy. Broilers that died spontaneously or that developed lameness were assigned to one of the following diagnostic categories: cull (runts and moribund individuals that failed to thrive); **UNK** (unknown cause of death); **SDS** (sudden death syndrome, flipover, heart attacks); **PHS** (pulmonary hypertension syndrome, ascites); **KB** (kinky back or spondylolisthesis: diagnosed based on the characteristic posterior paraparesis and hock-resting posture, and the absence of macroscopic BCO lesions; **TW** (twisted leg or slipped tendon, perosis, chondrodystrophy); **Normal F** (no macroscopic abnormalities of the proximal femur); **FHS** (proximal femoral head separation or epiphyseolysis); **FHT** (proximal femoral head transitional degeneration); **FHN** (proximal femoral head necrosis); **normal T** (no macroscopic abnormalities of the proximal tibia); **THN** (mild proximal tibial head necrosis, a subcategory of BCO in the tibiotarsus); **THNs** (severe THN in which the growth plate was imminently threatened or damaged); **THNc** (caseous THN in which caseous exudates or bacterial sequestrae were macroscopically evident); and **TD** (tibial dyschondroplasia). The BCO lesions encompass necrotic degeneration and microbial infection within the growth plates of and adjacent to the flexible T4 thoracic vertebra of broilers (e.g., spondylopathy or spondylitis, as well as in the proximal femoral and tibial growth plates; Riddell, 1973, 1976; Duff, 1990). Previously published photographs illustrate typical BCO lesions of the proximal femora and tibiae (Wideman et al., 2012; Wideman and Prisby, 2013). Proximal femoral head lesions (FHS, FHT, FHN) and tibial head lesions (THN, THNs, THNc) were categorized separately to emphasize the progressive development of BCO in the proximal ends of both long bones of the legs (Mutalib et al., 1983a; Thorp and Waddington, 1997; McNamee et al., 1998, 1999; Butterworth, 1999; McNamee and Smyth, 2000; Dinev, 2009; Durairaj et al., 2009; Wideman et al., 2012; Wideman and Pevzner, 2012). Proximal femora and tibiae that appeared to be normal macroscopically were not routinely evaluated microscopically. The total incidence of femoral BCO lesions was calculated as follows: total femur = FHS + FHT + FHN. The total incidence of tibial BCO lesions was calculated as follows: total tibia = THN + THNs + THNc. The total incidence of lameness was calculated as follows: total lame = KB + TW + TD + total femur + total tibia. For comparisons of lesion and lameness incidences, the individual bird was used as the experimental unit, and the SigmaStat Z-test procedure was used to compare proportions (Jandel Scientific, 1994, San Rafael, CA). In experiment 2, the SigmaStat ANOVA package was used to compare BW among experimental groups, treatments, and sexes. Clinically healthy survivors were not necropsied at the end of these experiments.

RESULTS

In both experiments the mortality through d 14 was <2% per cross. Between d 14 and 56, 3 birds in E1 and 8 birds in E2 were culled for poor performance. The remaining nonlame mortality was attributable to minor incidences of PHS and SDS that did not differ between sexes (not shown), floor treatments (not shown), or crosses (Table 1). In E1, one broiler was diagnosed as being lame for unknown reasons. Several birds initially appeared to have kinky back (spondylolisthesis); however, in every case the ensuing necropsies revealed BCO lesions of the proximal femora. Similarly, birds that initially appeared to be lame due to twisted leg or perosis were found to have severe unilateral BCO lesions of the proximal tibiae. In E2, one broiler was diagnosed as being lame for unknown reasons. Two lame birds were diagnosed as having kinky back (spondylolisthesis) based on their hock-resting posture and the absence of BCO lesions. Two birds that initially appeared to be lame due to twisted leg or perosis were found to have severe unilateral BCO of the proximal tibiae. Accordingly, ≥94% of the lameness observed in both experiments was attributable to lesions that are pathognomonic for BCO.

The incidence of lameness on litter flooring was low in both experiments and did not differ between sexes (not shown) or crosses. In E1, the incidence of total lameness for litter pens by cross was 4.4% (4/90) for W, 2.2% (2/90) for X, 3.3% (3/90) for Y, and 2.2% (2/90)

Table 1. Incidences of pulmonary hypertension syndrome (PHS, ascites) and sudden death syndrome (SDS, heart attacks, flipover) from 14 through 56 d of age for broilers from 4 commercial crosses in experiments 1 and 2 (sexes and floor treatments pooled per cross)

		Cause of mortality	
Experiment	Cross	PHS-ascites	SDS
1	W	0.3% (1/330)	0.9% (3/330)
1	X	0.6% (2/330)	1.8% (6/330)
1	Y	1.2% (4/330)	0.9% (3/330)
1	Z	0.9% (3/330)	1.2% (4/330)
2	W	0.5% (2/390)	1.8% (7/390)
2	X	0.2% (1/390)	1.0% (4/390)
2	Y	0.5% (2/390)	0.8% (3/390)
2	Z	0.2% (1/390)	1.0% (4/390)

for Z ($P \geq 0.6$). In E2, the incidence of total lameness for litter pens by cross was 4.6% (6/130) for W, 3.1% (4/130) for X, 3.8% (5/130) for Y, and 2.3% (3/130) for Z ($P \geq 0.8$). Figures 2 to 4 illustrate the time course of cumulative lameness for broilers reared in pens with wire flooring in E1 (upper panels) and E2 (lower panels). Beginning on d 36 (E1) or d 46 (E2) males from cross Y consistently had higher incidences of cumulative lameness than males from all other crosses. On d 56 of both experiments, males from cross W had higher incidences of cumulative lameness than males from cross X, and the incidences for males from crosses X and Z did not differ (Figure 2). The cumulative lameness incidences differed by cross among females in E1, with females from cross Y developing a higher incidence by d 56 than females from cross W, which in turn had a higher incidence than females from crosses X and Z (Figure 3, upper panel). In contrast, throughout E2 the females of all 4 crosses developed similar lameness incidences (Figure 3, lower panel). When the data for males and females were combined, broiler cross Y consistently developed the highest incidence of lameness compared with crosses W, X, and Z (Figure 4). Cumulative lameness incidences are compared between sexes and crosses, or between crosses independent of sex in Figure 5 and Table 2. In E1, males from cross Y developed the highest incidence of lameness, followed by males from cross W and females from cross Y. Females from crosses X and Z had the lowest susceptibility to lameness when reared on wire flooring (Figure 5, upper panel). In E2, the cumulative lameness incidences for females were low and did not differ among the crosses (W = 16.2%, X = 14.6%, Y = 16.2%, Z = 14.6%). Among males, the incidence of lameness was higher for cross Y than for cross W, which in turn had a higher incidence than cross X (Figure 5, lower panel). When the sexes were pooled, broilers from cross Y developed more lameness than broilers from cross W in both experiments (Figure 5, Table 2).

Body weights were not recorded in E1 but were recorded on d 35 and 56 in E2, as illustrated by cross and sex in Figure 6. On d 35, the males from cross Y were heavier than males from cross W, which in turn were heavier than males from cross X. Also, on d 35 the females from all crosses weighed less than the males from their respective crosses, and females from crosses W and Y were heavier than females from crosses X and Z. On d 56, the males from cross Y were heavier than males from cross X, but did not differ compared with males from crosses W and Z. The females on d 56 weighed less than the males from their respective crosses, but among females the BW did not differ by cross.

Figures 7 and 8 illustrate the incidences within the proximal femoral and tibial head diagnostic categories when the data for all lame broilers were pooled by leg (all right vs. all left leg comparisons) or by sex (all females vs. all males) independent of cross. In E1, there were no differences within the femoral diagnostic categories, whereas in E2 the right vs. left leg comparisons revealed a solitary difference for FHN. Also, in E2 lame females had slightly higher incidences of normal femora and lower incidences of total femoral lesions (FHS + FHT + FHN) compared with lame males (Figure 7). With regard to the tibial diagnostic categories, in E1 right legs had higher incidences of THN and lower incidences of THNs compared with left legs. Otherwise, there were no differences in tibial lesion incidences between right and left legs. In both experiments, lame females tended to have fewer normal tibiae and more total tibial lesions (all THN) when compared with lame males (Figure 8). Overall, neither the leg nor sex markedly affected the femoral or tibial patterns of BCO lesion development in lame broilers.

The proximal femoral head diagnostic categories are compared for lame broilers from each cross in Figure 9. In both experiments, differences were observed in every category except FHT. The overall patterns suggest that wire flooring induced lameness associated with substantial susceptibility to femoral head damage in all 4 crosses (e.g., FHS + FHT + FHN). Paradoxically, broiler cross Y had the highest incidence of total lameness (Figure 5), but nevertheless had the highest incidence of normal femora and low incidences of FHN and FHS + FHT + FHN compared with the other crosses in E1. In E2, cross W had a higher incidence of normal femora and a lower incidence of total femoral lesions than cross Y (Figure 9). The proximal tibial head diagnostic categories for lame broilers from all 4 crosses are compared in Figure 10. In both experiments, the differences between crosses were minimal.

DISCUSSION

Growing broilers on wire flooring provides a reliable experimental model for reproducibly triggering significant levels of lameness attributable to lesions that are pathognomonic for BCO (Wideman et al., 2012; Wideman and Prisby, 2013). Wire flooring imposes a rigorous, sustained challenge that undoubtedly is much more severe than typically would be experienced under normal commercial conditions. Indeed, the incidences of lameness for broilers reared on litter are very modest compared with the significantly amplified incidences that routinely are elicited when hatch-mates are reared on wire flooring. In the present study, the primary objective was to determine if 4 commercial broiler crosses having innately different patterns of early growth also differed in their susceptibility to BCO. Broiler integrators familiar with these crosses would expect "standard" crosses W and Y to grow very rapidly at an early age whereas the "yield" crosses X and Z would initially grow more slowly. Based on the consensus hypothesis that leg disorders and lameness develop because the skeleton fails to mature rapidly enough to support maximum rates of BW accretion, we expected crosses W and Y to develop higher incidences of lameness than crosses X and Z. The anticipated differences in patterns of BW gain were observed in both experiments, and

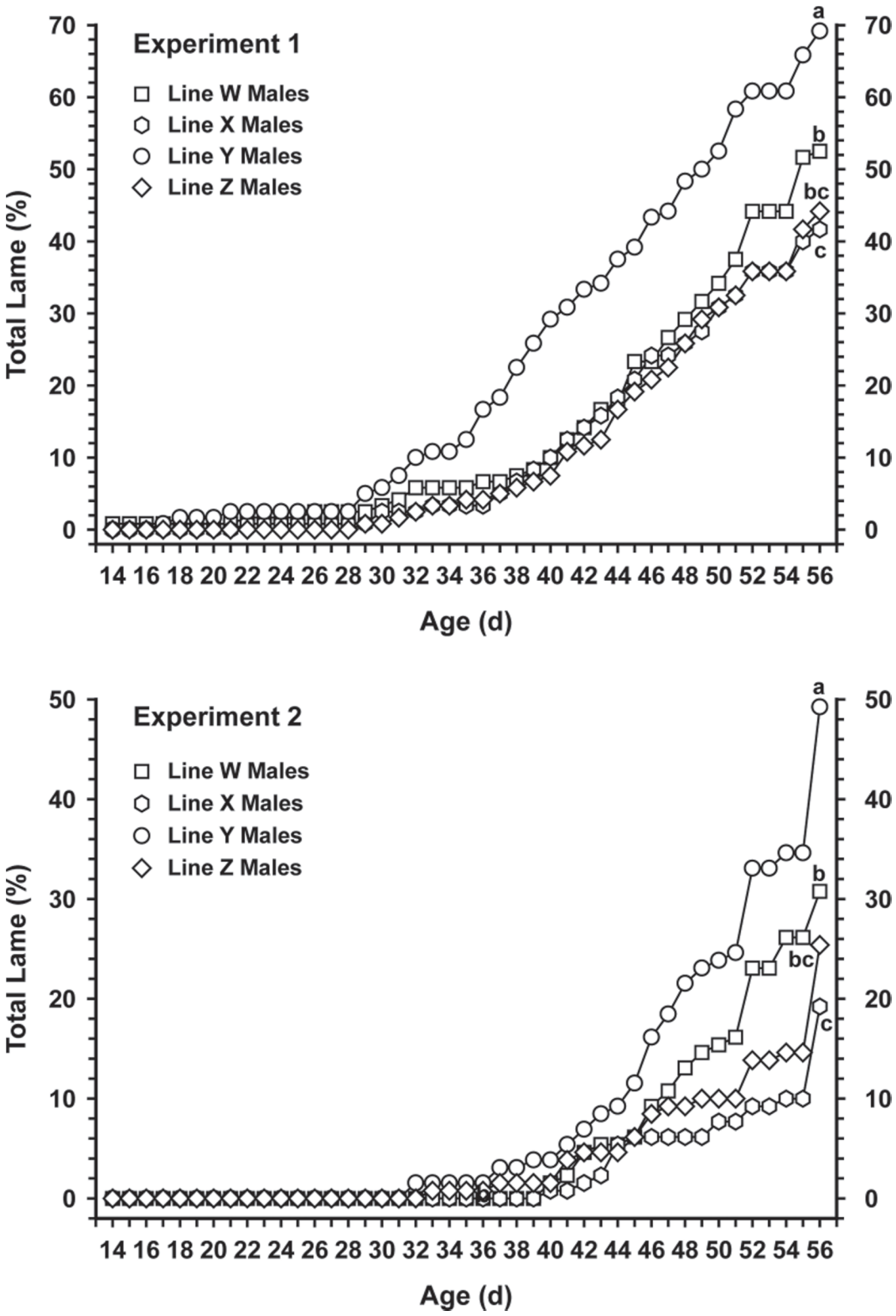

Figure 2. Time course of cumulative total lameness for male broilers from crosses W, X, Y, and Z that were reared in pens with wire flooring in experiment (E) 1 (upper panel) and E2 (lower panel). Values are calculated as the percentage of the total number of males on wire flooring per line on d 14. [a–c]Values differed between the crosses within a day ($P \leq 0.05$; SigmaStat Z-Test). Note different scales for the y-axes.

were quantified in E2. Accordingly, within each sex on d 35, the "standard" crosses W and Y had a higher average BW than their companion "yield" crosses X and Z, respectively, whereas by d 56 the "standard" crosses no longer had significantly higher BW compared with their companion "yield" crosses (Figure 6). These relative differences in early growth performance were consistent with relative differences in the cumulative total lameness among the 4 crosses, particularly among males (Figure 5). In both experiments males from cross

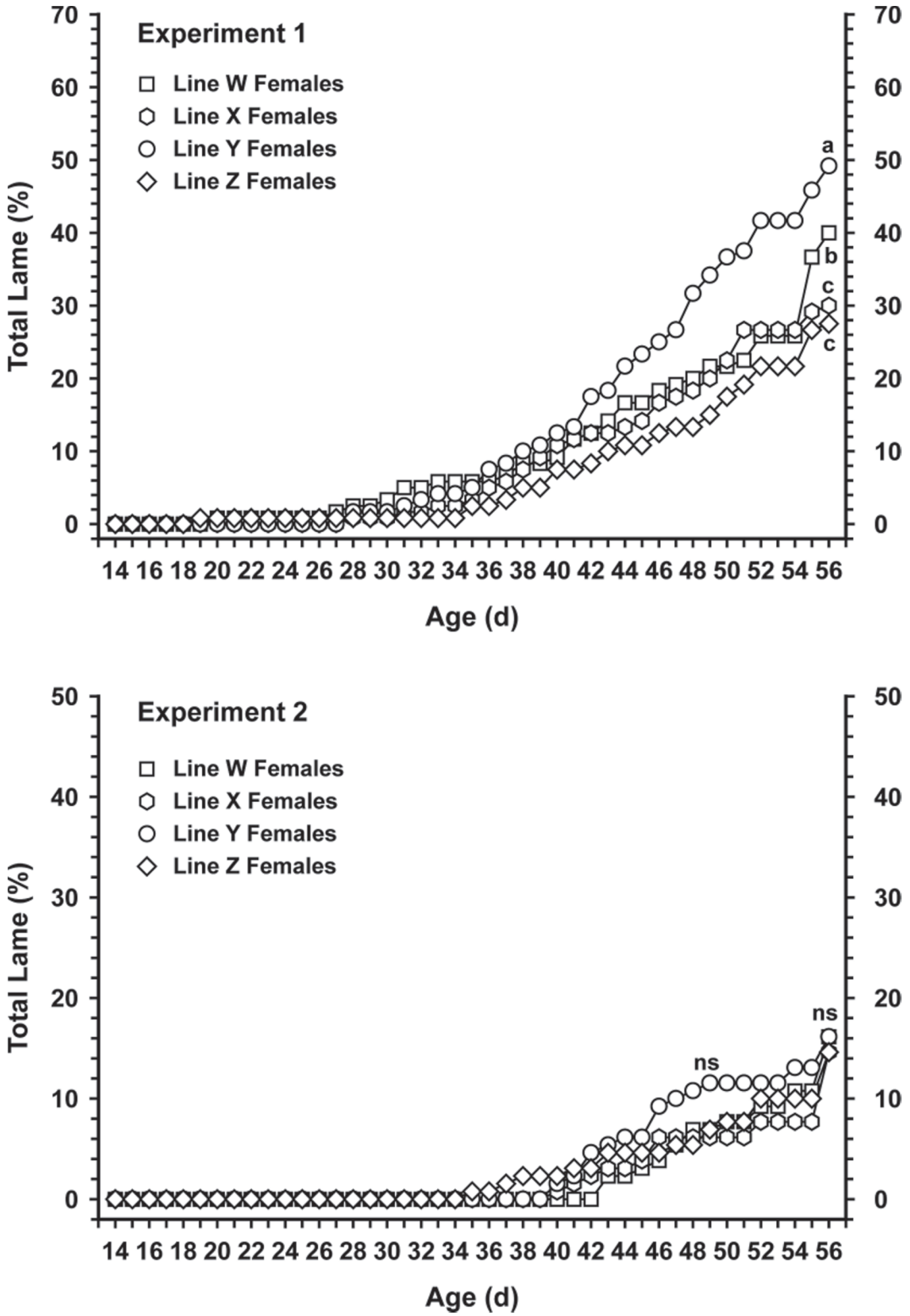

Figure 3. Time course of cumulative total lameness for female broilers from crosses W, X, Y, and Z that were reared in pens with wire flooring in experiment (E) 1 (upper panel) and E2 (lower panel). Values are calculated as the percentage of the total number of females on wire flooring per line on d 14. [ns]None of the values differed between crosses ($P > 0.05$; SigmaStat Z-test). [a–c]Values differed between the crosses within a day ($P \leq 0.05$; SigmaStat Z-Test). Note different scales for the y-axes.

Y exhibited the highest incidences of lameness, followed in numerical order by males from crosses W, Z, and X. Within each cross, the females grew more slowly than males, and within each cross the females were less likely than males to develop lameness. McNamee et al. (1999) previously reduced the incidence of BCO in broilers exposed to aerosolized *Staphylococcus aureus* by restricting feed to 60% of ad libitum intake. The available

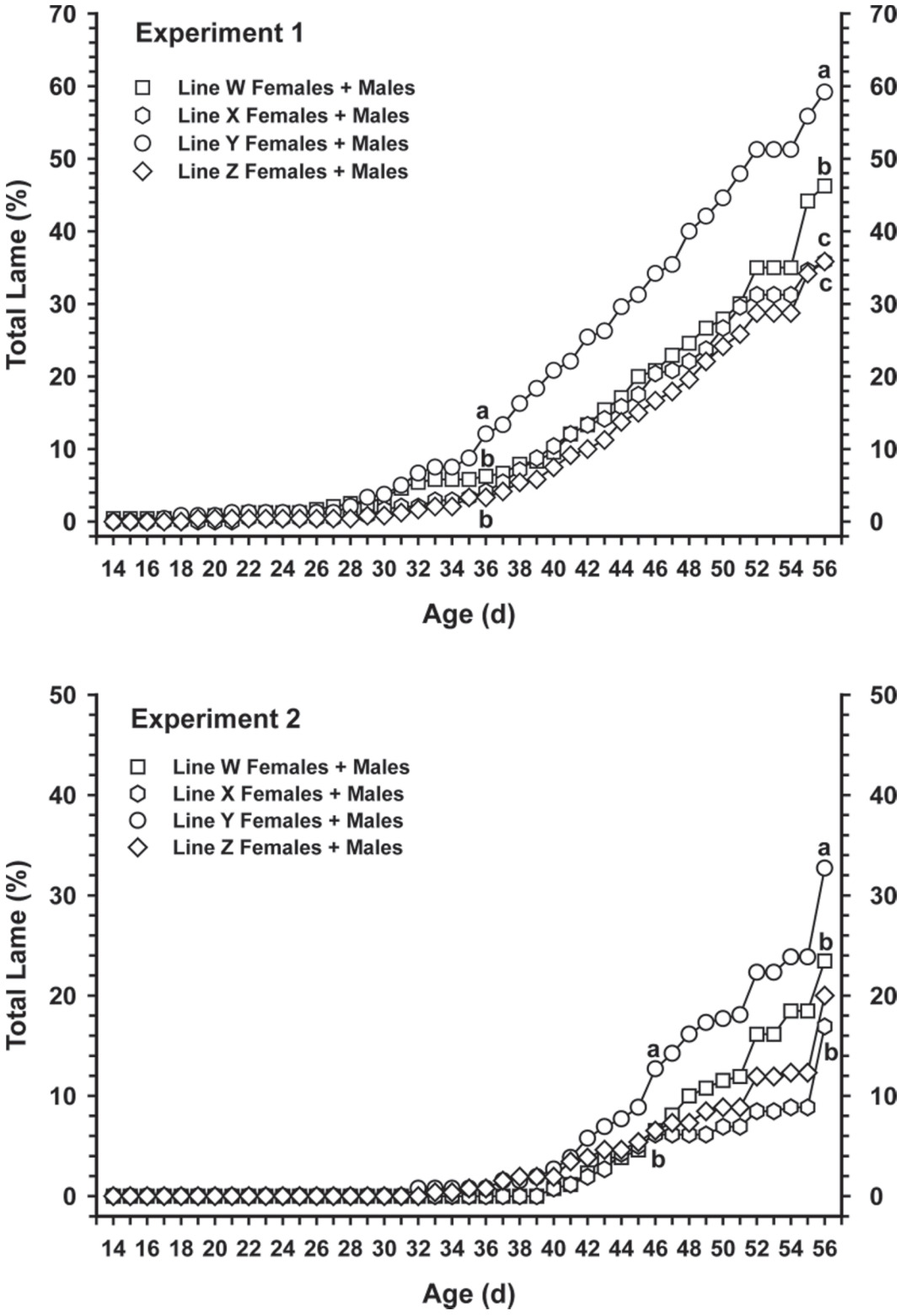

Figure 4. Time course of cumulative total lameness for female and male broilers from crosses W, X, Y, and Z in experiment (E) 1 (upper panel) and E2 (lower panel). Values are calculated as the percentage of the total number of birds on wire flooring per line on d 14. [a–c]Values differed between the crosses within a day ($P \leq 0.05$; SigmaStat Z-test). Note different scales for the y-axes.

evidence therefore supports the hypothesis that rapid early growth predisposes broilers to develop BCO, in concurrence with the tendency for rapid growth to impair walking ability and amplify the incidences of other etiologically independent leg disorders in poultry (see Introduction).

Experiments 1 and 2 were conducted under putatively similar environmental, nutritional, and management

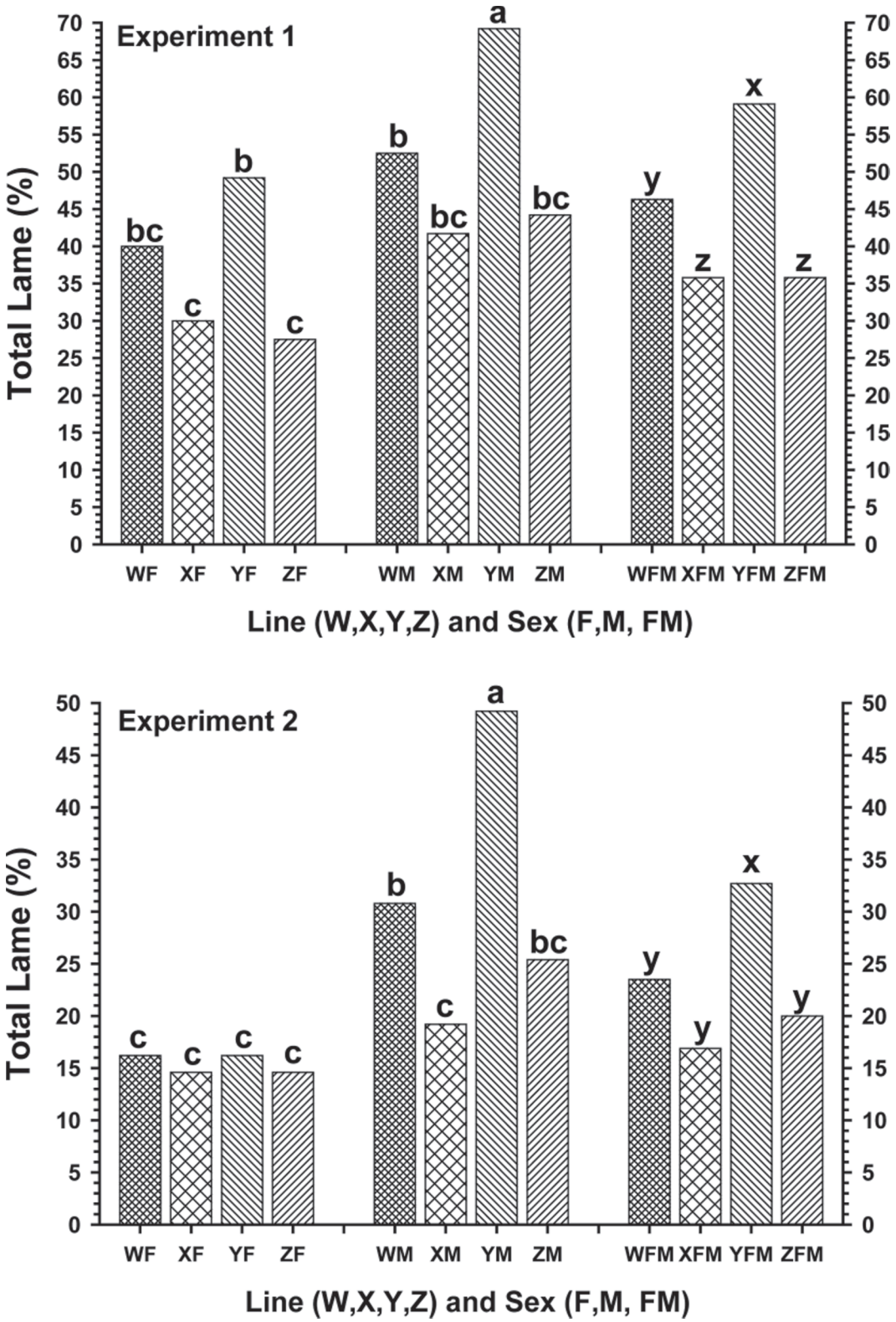

Figure 5. Cumulative total lameness on d 56 for female (F) and male (M) broilers from crosses W, X, Y, and Z in experiment (E) 1 (upper panel) and E2 (lower panel). Note different scales for the y-axes. [a–c]Values differed among lines and sexes; [x–z]values differed among lines with the sexes combined ($P \leq 0.05$; SigmaStat Z-Test).

conditions. In both experiments, the numerical ranking of susceptibility to BCO remained consistent for males from the 4 crosses: X ≤ Z ≤ W < Y. A similar numerical ranking was observed for females in E1. However, the incidences of BCO within each cross and sex were lower in E2 than in E1, and in E2 the female broilers from all 4 crosses exhibited low incidences of BCO (Figure 5). Two factors may have differentially influenced these

Table 2. Cumulative total incidences of lameness through d 56 on wire flooring for female broilers, male broilers, and females and males combined from crosses W, X, Y, and Z for experiments 1, 2, and 1 and 2 combined

		Sex		
Experiment	Cross	Females % (n lame/n total)	Males % (n lame/n total)	Females + males % (n lame/n total)
1	W	40.0 (48/120)^{b,x}	52.5 (63/120)^{b,x}	46.3 (111/240)^{b,x}
	X	30.0 (36/120)^{c,x}	41.7 (50/120)^{c,x}	35.8 (86/240)^{c,x}
	Y	49.2 (59/120)^{a,y}	69.2 (83/120)^{a,x}	59.1 (142/240)^{a,xy}
	Z	27.5 (33/120)^{c,y}	44.2 (53/120)^{bc,x}	35.8 (86/240)^{c,xy}
2	W	16.2 (21/130)^{a,y}	30.8 (40/130)^{b,x}	23.5 (61/260)^{b,xy}
	X	14.6 (19/130)^{a,x}	19.2 (25/130)^{c,x}	16.9 (44/260)^{b,x}
	Y	16.2 (21/130)^{a,z}	49.2 (64/130)^{a,x}	32.7 (85/260)^{a,y}
	Z	14.6 (19/130)^{a,y}	25.4 (33/130)^{bc,x}	20.0 (52/260)^{b,xy}
1 and 2	W	27.6 (69/250)^{ab,y}	41.2 (103/250)^{b,x}	34.4 (172/500)^{b,xy}
	X	22.0 (55/250)^{b,y}	30.0 (75/250)^{c,x}	26.0 (130/500)^{c,xy}
	Y	32.0 (80/250)^{a,z}	58.8 (147/250)^{a,x}	45.4 (227/500)^{a,y}
	Z	20.8 (52/250)^{b,y}	34.4 (86/250)^{bc,x}	27.6 (138/500)^{c,x}

$^{a–c}$Values differed between crosses within an experiment and column (sex; $P \leq 0.05$; Sigma Stat Z-test).

$^{x–z}$Values differed between sexes within an experiment and row (cross; $P \leq 0.05$; Sigma Stat Z-test).

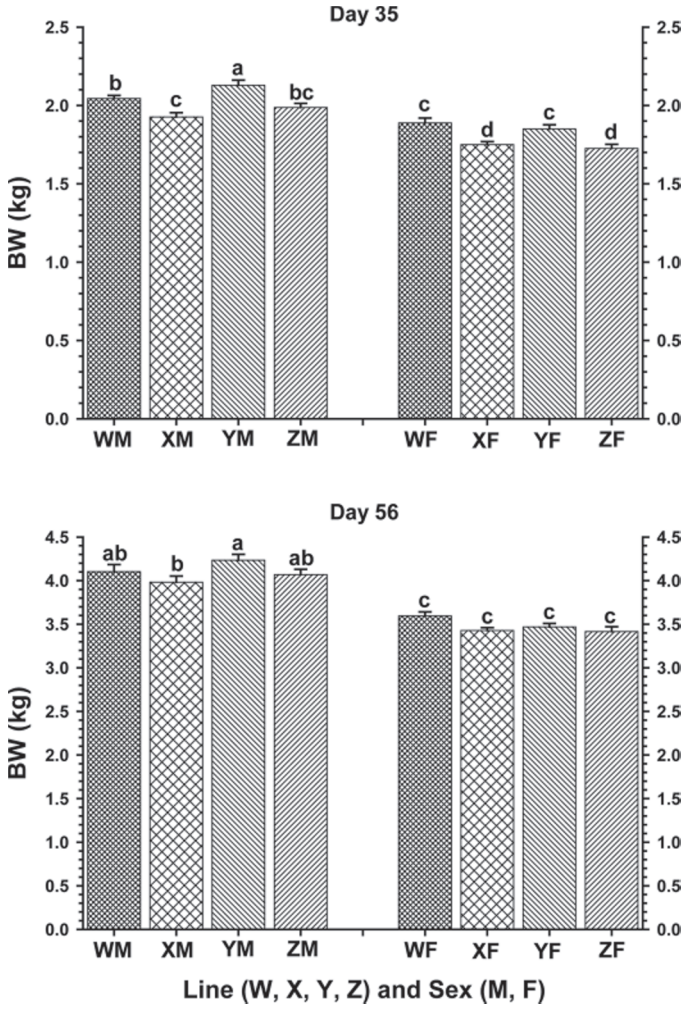

Figure 6. Body weights for clinically healthy male (M) and female (F) broilers from crosses W, X, Y, and Z in experiment 2 on d 35 (upper panel) and d 56 (lower panel). Note different scales for the y-axes. $^{a–d}$Values differed between lines and sexes within an age ($P \leq 0.05$; SigmaStat Z-test).

outcomes. First, all chicks used in E1 were obtained from a commercial hatchery, whereas all chicks for E2 were hatched at the University of Arkansas Poultry Research Farm. Hatchery sanitation and management have been implicated as factors that potentially may influence the incidence of BCO (see Introduction). It also has been our experience that transporting chicks from distant hatcheries imposes significant additional shipping stress contributing to elevated incidences of cull chicks, increased early mortality, and lameness attributable to osteomyelitis beginning during the first week. Our wire flooring research protocols rapidly evolved to include heavy culling of the weakest chicks on d 14, thereby helping to minimize the early onset of BCO that we currently attribute to hatchery issues and shipping stress (Wideman et al., 2012). In both of the present studies the chicks were culled heavily at the end of the second week; nevertheless, the time course depictions show lameness beginning as early as d 18 in E1, but not until d 32 in E2 (Figures 2 to 4). Lines or experimental groups of broilers that exhibit an earlier onset of BCO subsequently tend to develop higher cumulative incidences of lameness when compared with lines or groups in which the onset of lameness is delayed to substantially later ages.

Another factor that may have differentially influenced these experiments was rearing the chicks "straight-run" in E1 vs. sex-separate in E2. Previously we reared the sexes straight-run, and incidences of lameness for females tended to be only moderately lower than for males (Wideman et al., 2012; R. F. Wideman Jr., unpublished observations). Experiment 2 of the present study was the first instance in which we reared the sexes separately on wire flooring. In this experiment the females developed uniformly low incidences of BCO, and the anticipated differences between "standard" vs. "yield" crosses failed to materialize (Figures 3 and 5, lower panels) in spite of the fact that the females from crosses W and Y did exhibit faster early growth compared with

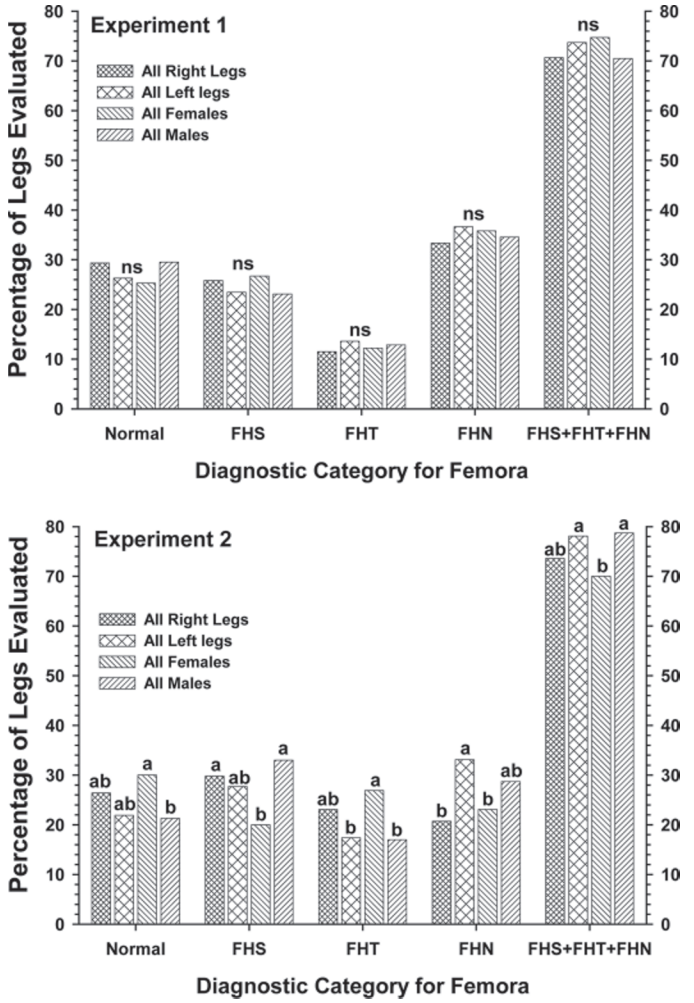

Figure 7. Incidences within proximal femoral head diagnostic categories for lame broilers that were reared on wire flooring in experiment (E) 1 (upper panel) and E2 (lower panel). All crosses and sexes were pooled for right vs. left leg comparisons. All crosses and both legs were pooled for female vs. male comparisons. The proximal femoral heads of both legs were evaluated and were diagnosed as being macroscopically normal (normal femur; no apparent abnormalities) or they exhibited FHS (femoral head separation), FHT (femoral head transitional degeneration), or FHN (femoral head necrosis). Total femoral head lesions = FHS + FHT + FHN. Values reflect the percentages of all legs evaluated: in E1, n = 436, 436, 358, and 514 for all right legs, all left legs, all legs from females, and all legs from males, respectively; in E2, n = 242, 242, 160, and 324 for all right legs, all left legs, all legs from females, and all legs from males, respectively. [ns]None of the values differed within a diagnostic category ($P \geq 0.05$; SigmaStat Z-test). [a,b]Values differed between legs and sexes within a diagnostic category ($P \leq 0.05$; SigmaStat Z-test).

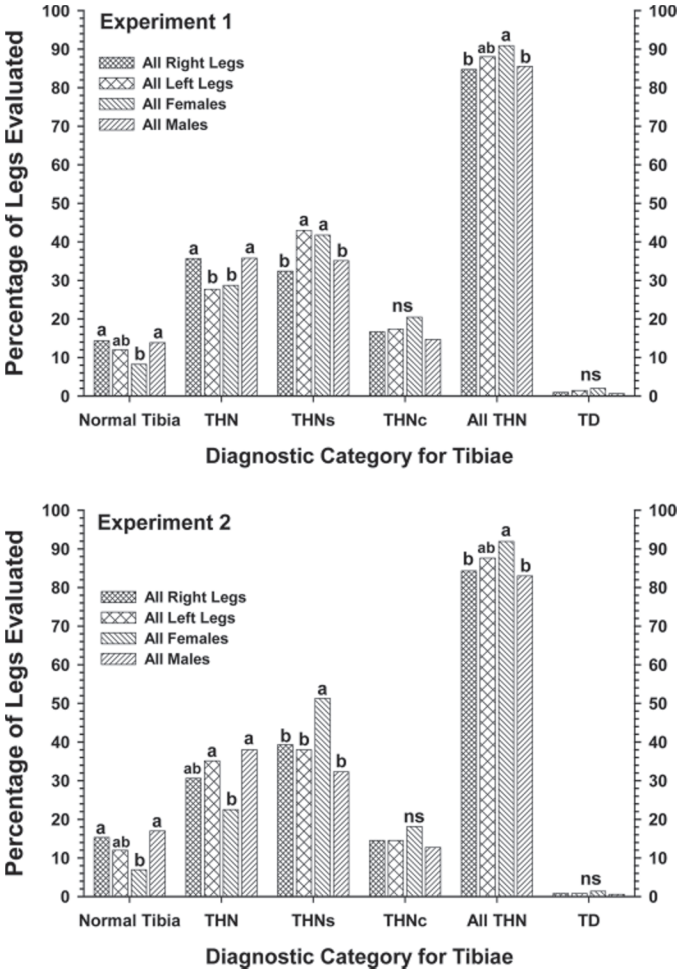

Figure 8. Incidences within proximal tibial head diagnostic categories for lame broilers that were reared on wire flooring in experiment (E) 1 (upper panel) and E2 (lower panel). All crosses and sexes were pooled for right vs. left leg comparisons. All crosses and both legs were pooled for female vs. male comparisons. The proximal tibial heads of both legs were evaluated and were diagnosed as being macroscopically normal (no apparent abnormalities) or they exhibited THN (mild proximal tibial head necrosis, a subcategory of bacterial chondronecrosis with osteomyelitis in the tibiotarsus), THNs (severe THN in which the growth plate was imminently threatened or damaged), THNc (caseous THN in which caseous exudates or bacterial sequestrae were macroscopically evident), or TD (tibial dyschondroplasia). Total tibial head lesions (all THN = THN + THNs + THNc + TD). Values reflect the percentages of all legs evaluated: in E1, n = 436, 436, 358, and 514 for all right legs, all left legs, all legs from females, and all legs from males, respectively; in E2, n = 242, 242, 160, and 324 for all right legs, all left legs, all legs from females, and all legs from males, respectively. [ns]None of the values differed within a diagnostic category ($P \geq 0.05$; SigmaStat Z-test). [a,b]Values differed between legs and sexes within a diagnostic category ($P \leq 0.05$; SigmaStat Z-test).

crosses X and Z (Figure 6). It is possible that female broilers experience less social/psychological or physical/competitive stress when reared separately from their male hatch mates, thereby attenuating a source of sustained stress that otherwise could aggravate the pathogenesis of BCO. This phenomenon will be reassessed in future studies. If the observation can be confirmed, then sex-separate rearing would constitute an immediate strategy for reducing the overall incidence of lameness in commercial flocks. It also can be inferred that selecting broilers for reduced overall perception of or responsiveness to environmental or social stressors should also improve their innate resistance to BCO. Rapid growth, per se, might be considered a stressor. With regard to the likelihood of continued genetic improvement in broilers' innate resistance to BCO, it is encouraging to note that in all 4 commercial broiler crosses numerous large, robust, clinically healthy males and females did survive the rigorous, sustained wire flooring challenge through d 56.

Pathognomonic BCO lesions develop predominately in the proximal femoral and tibial growth plates and

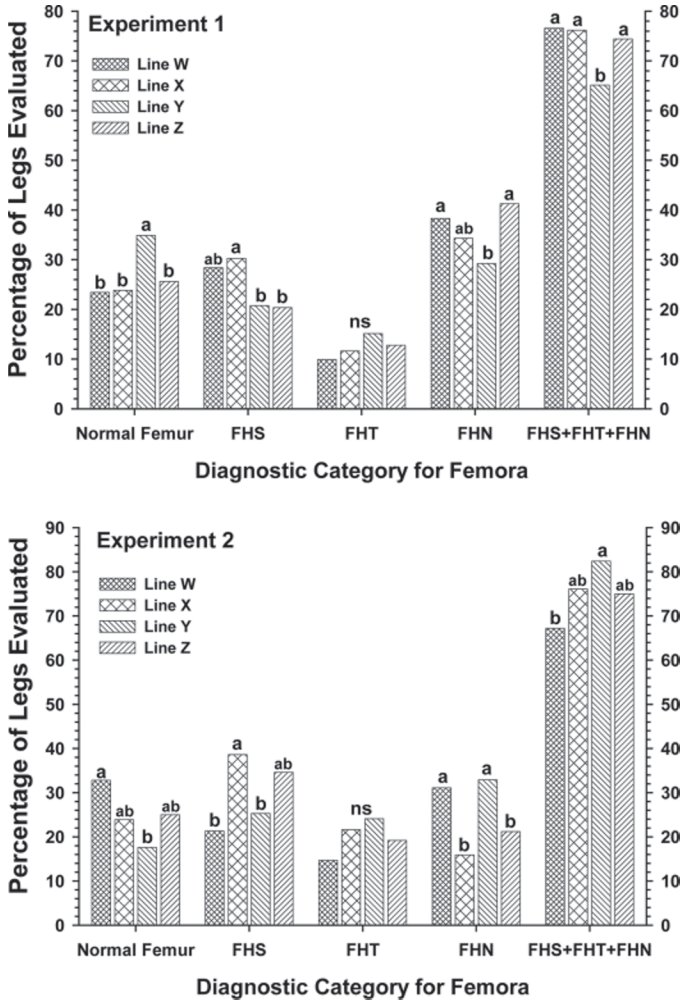

Figure 9. Incidences within proximal femoral head diagnostic categories for lame broilers from crosses W, X, Y, and Z that were reared on wire flooring in experiment (E) 1 (upper panel) and E2 (lower panel). Note different scales for the y-axes. The proximal femoral heads of both legs were evaluated and were diagnosed as being macroscopically normal (normal femur; no apparent abnormalities) or they exhibited FHS (femoral head separation), FHT (femoral head transitional degeneration), or FHN (femoral head necrosis). Total femoral head lesions = FHS + FHT + FHN. Values reflect the percentages of all legs evaluated (right and left legs pooled; sexes pooled): in E1, n = 222, 172, 284, and 172 for crosses W, X, Y, and Z, respectively); in E2, n = 122, 88, 170, and 104 for lines W, X, Y and Z, respectively. [ns]None of the values differed within a diagnostic category ($P \geq 0.05$; SigmaStat Z-test). [a,b]Values differed between crosses within a diagnostic category ($P \leq 0.05$; SigmaStat Z-test).

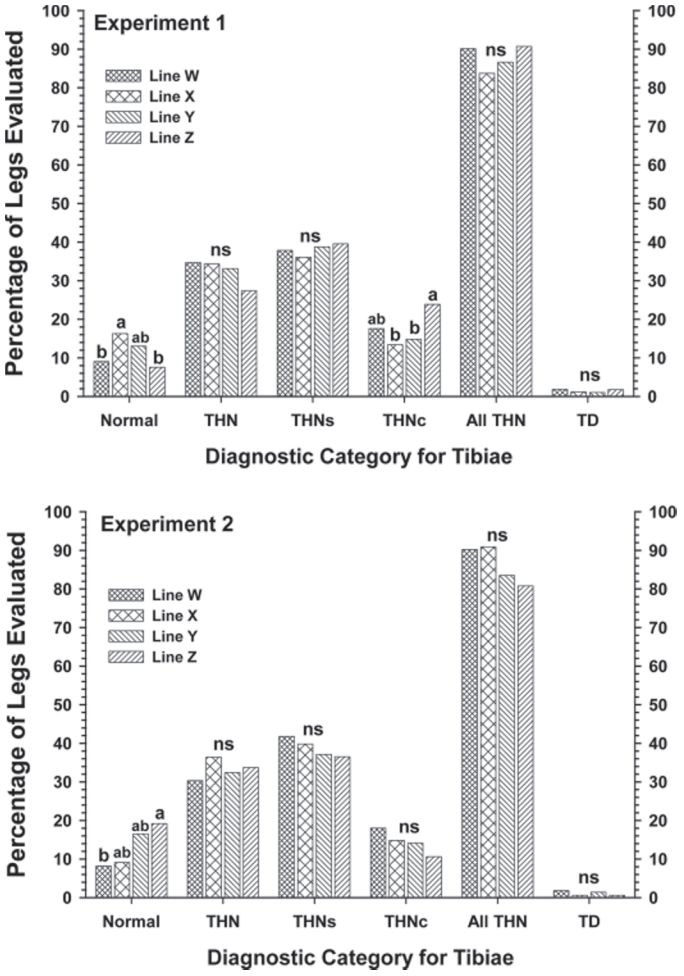

Figure 10. Incidences within proximal tibial head diagnostic categories for lame broilers from crosses W, X, Y, and Z that were reared on wire flooring in experiment (E) 1 (upper panel) and E2 (lower panel). The proximal tibial heads of both legs were evaluated and were diagnosed as being macroscopically normal (no apparent abnormalities) or they exhibited THN (mild proximal tibial head necrosis, a subcategory of bacterial chondronecrosis with osteomyelitis in the tibiotarsus), THNs (severe THN in which the growth plate was imminently threatened or damaged), THNc (caseous THN in which caseous exudates or bacterial sequestrae were macroscopically evident), or TD (tibial dyschondroplasia). Total tibial head lesions (all THN) = THN + THNs + THNc. Values reflect the percentages of all legs evaluated (right and left legs pooled; sexes pooled): in E1, n = 222, 172, 284, and 172 for crosses W, X, Y, and Z, respectively; in E2, n = 122, 88, 170, and 104 for lines W, X, Y, and Z, respectively. [ns]None of the values differed within a diagnostic category ($P \geq 0.05$; SigmaStat Z-test). [a,b]Values differed between crosses within a diagnostic category ($P \leq 0.05$; SigmaStat Z-test).

metaphyses rather than at the distal ends of the same bones (Wideman et al., 2012), likely reflecting the observation that proximal growth plates elongate the leg bones twice as rapidly as distal growth plates (Church and Johnson, 1964). The rate of leg bone elongation is directly proportional to the width of the growth plate, which in turn represents the product of the mitotic rate in the proliferating zone multiplied by the magnitude of cellular enlargement or swelling in the hypertrophic zone (Lutfi, 1970a; Kember and Kirkwood, 1987; Thorp, 1988; Kirkwood et al., 1989a,b; Kember et al., 1990; Farquharson et al., 1992, 1993; Hurwitz et al., 1992). Accordingly, the columns of poorly aligned and unmineralized hypertrophic chondrocytes are thicker in the proximal growth plate compared with the distal growth plate, thereby creating an amplified predisposition for microfracturing and cleft formation (osteochondrosis) within the proximal physeal cartilage (Thorp, 1988; Kirkwood et al., 1989a). In the present study, proximal femoral and tibial lesion incidences in lame birds differed only minimally for left vs. right leg comparisons, and for male vs. female comparisons in both E1 and E2, as was observed previously (Wideman et al., 2012). Furthermore, although cumulative lameness

did differ among the 4 broiler crosses, for birds that became lame the proximal femoral and tibial lesion incidences and distributions remained remarkably consistent between the crosses. Accordingly, it is difficult to attribute the specific lesion patterns of lame broilers per se to traits commonly considered to differentiate the 4 commercial crosses, such as patterns of growth, leg conformation, stance, gait, or overall body morphometrics. Instead, the femoral and tibial lesion distributions must be considered to be broadly pathognomonic for BCO. Factors contributing to different BCO susceptibilities among broiler crosses most likely are related to differences in the biological mechanisms associated with lesion initiation and persistence (e.g., early growth rates, growth plate thickness, susceptibility to physeal osteochondrosis, chronic ischemia, bacterial translocation, immunological competence, responsiveness to perceived stress) rather than to the subsequent progression or proportional distribution of pathognomonic BCO lesions (Wideman and Prisby, 2013).

In conclusion, BCO is widely considered to be the most common cause of lameness in commercial broilers worldwide. Rearing broilers on wire flooring imposes a rigorous challenge that consistently triggers high incidences of BCO. The efficacy of wire flooring likely includes both amplified mechanical stress contributing to proximal physeal damage, as well as chronic physiological stress contributing to ischemic necrosis and immunosuppression that are permissive for bacterial translocation and proliferation. Rapid early growth has been linked to enlarged, structurally unstable growth plates in the proximal femora and tibiae, which theoretically predispose "standard" broiler crosses to greater susceptibility to BCO compared with "yield" crosses. Indeed, in 2 independent experiments broilers from standard crosses that grew rapidly at an early age developed higher incidences of BCO compared with their companion "yield" crosses that initially tended to grow more slowly. Within each cross, male broilers grew more rapidly and developed higher incidences of BCO compared with female broilers. Regardless of cross, birds that developed BCO had remarkably consistent patterns of proximal femoral and tibial lesion incidences and distributions. Accordingly, the femoral and tibial lesions must be considered to be pathognomonic for BCO instead of being attributable to traits that specifically differentiate the 4 crosses. Finally, females (but not males) reared separately on wire flooring unexpectedly developed uniformly low incidences of BCO, regardless of cross. Stress-mediated immunosuppression contributes to the pathogenesis of BCO; perhaps female broilers experience less social or competitive stress when reared separately from their male hatch mates.

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