PHYSIOLOGY AND REPRODUCTION

Effects of Fenfluramine on Body Weight, Feed Intake, and Reproductive Activities of Broiler Breeder Hens

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ABSTRACT Inherited overfeeding and fattiness reduce laying performance in broiler breeder pullets. Although feed restriction is used to compensate for overeating and weight gain, this management practice leads to increases in BW variation, labor cost, and bird stress. Dietary supplementation of anorectic agents, such as fenfluramine, may be an alternative. Anak female prebreeder hens (19 wk of age; n = 10 per group) were treated as follows: daily oral administration of 5, 10, 20, or 40 mg DL-fenfluramine/kg BW or saline with food provided for *ad libitum* intake or administration of saline and feed restriction. Daily feed intake (FI), laying rate, egg composition, and BW were measured. At 40 wk of age, adipose tissue and ovary weights were measured. Fenfluramine depressed ($P < 0.05$) BW and FI in a dose-dependent manner, but was less effective in reducing BW than feed restriction. Suppression of FI occurred in two phases: a dynamic phase, coinciding with the rapid growth phase, during which FI declined progressively and a static phase during which FI reached a plateau at a significantly low level until the end of the experimental period. Egg production peaked first in saline-treated hens fed for *ad libitum* intake, but soon after started to decline. In all fenfluramine-treated and feed-restricted hens, egg production peaked 3 to 4 wk later and remained high until the end of the experiment. There were no differences in egg and egg component weights among the experimental groups. Abdominal adipose tissue weight was reduced by fenfluramine in a dose-related manner, and its weight in the group treated with the highest dose was similar to that of feed-restricted hens. In these two groups, ovarian weight was significantly higher than in the saline-treated hens fed for *ad libitum* intake, and a small, nonsignificant increase in ovary size was observed in groups treated with the two median doses of fenfluramine. The effect of fenfluramine on egg production was similar to that of feed restriction, but it was not dose-dependent and, thus, not directly related to its leaning effect. In broiler breeder hens, oral fenfluramine may be used for chemical feed restriction and diminution of fattiness without reducing egg production relative to manually feed-restricted hens.

(*Key words*: broiler breeder, body weight, fenfluramine, feed consumption)

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INTRODUCTION

Broiler breeder females manifest the inherent ability to grow rapidly and, when consuming feed for *ad libitum* intake, they gain excessive BW and become fatty. Prevention of fattiness in broiler breeder pullets is essential for achieving the desired reproductive performance because obesity decreases egg production and fertility, whereas feed is consumed in higher amounts to maintain the excessive body mass. In addition, *ad libitum* feeding can cause multiple ovulations, resulting in double yolks and poorly shelled eggs, which are considered as discarded incubator eggs (Hocking *et al.*, 1987).

Feed restriction is commonly used to control growth rate and to prevent fattiness in pullets. Various methods of physical feed restriction have been used commercially: skip 1 d (Leeson and Summers, 1985; Wilson *et al.*, 1989), skip 2 d (Bartov *et al.*, 1988), and daily feed restriction (Leeson and Summers, 1985; Wilson *et al.*, 1989). All manual feed restrictions are associated with intensive labor and increased BW variation, and they may be an undesirable stressor. Supplementation of anorectic agents to the breeder pullet diet may alleviate the disadvantages of manual feed restriction and still prevent fattiness. Because it is simpler than manual feed restriction, it may also reduce labor and special equipment required for dosed feed restriction. However, some anorectic agents have

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Abbreviation Key: DF = D-fenfluramine; FI = feed intake; 5-HT = serotonin.

been found to have deleterious effects during the laying period (Oyawoye and Krueger, 1986; Hussien *et al.*, 1989).

Fenfluramine is well known for its anorectic properties (Rowland and Carlton, 1986) and has been used as an appetite suppressant in humans. D-Norfenfluramine and its parent compound D-fenfluramine (DF) suppress feeding by releasing endogenous serotonin (5-HT) in the brain, mimicking the natural release of 5-HT during satiation that terminates feeding (Mennini *et al.*, 1985). Injection of DF at the dose of about 0.5 mg/kg BW produces general suppression of feeding all macronutrients in rats (Weiss *et al.*, 1990).

In 40-wk-old layer strain chickens, i.m. injections of DL-fenfluramine at 10 mg/kg BW resulted in a significant reduction in feed intake (FI) and increased metabolic rate and heat loss (MacLeod *et al.*, 1992). Reduced energy input coupled with increased energy output led to reduced fattiness. Furthermore, fenfluramine injections to broiler breeder hens and growing broilers caused a dose-dependent reduction in feed intake and BW (Hocking and Bernard, 1993).

In the present study, we assayed the effect of orally administered DL-fenfluramine on FI, fattiness, and egg laying rate in broiler breeder hens.

MATERIALS AND METHODS

Animals

Sixty 19-wk-old Anak female prebreeder hens (Israeli Breeder Union) were housed in an open-sided chicken house equipped with individual cages and individual feeders. Upon arrival, birds were weighed, wing-banded, and fed according to the Israeli Breeder Union Manual [i.e., 100 g prebreeder feed/d (17% protein) until 22 wk of age, when the experiment was started]. Supplementation of artificial light was according to the Israeli Breeder Union Manual (i.e., photostimulation beginning at 22 wk of age and reaching 16 h of light at peak egg production by 30 wk of age).

Treatment Groups

Treatment groups were as follows: 1) daily oral administration at noon by intubation of 5, 10, 20, or 40 mg DL-fenfluramine[2]/kg BW dissolved in water (FEN 5, 10, 20, and 40, respectively; 2) *ad libitum* (control) feed intake plus oral administration with the same volume of saline; 3) feed restriction (restricted control) orally administered with the same volume of saline.

Feed restriction was according to the Israeli Breeder Union Manual, starting at 100 g feed/bird per d ending at 140 g/bird per d by the end of the experiment. Birds of the different experimental groups were randomly located in the same laying battery marked individually for each fenfluramine treatment.

[2]Sigma Chemical Co., St. Louis, MO 63178-9916.

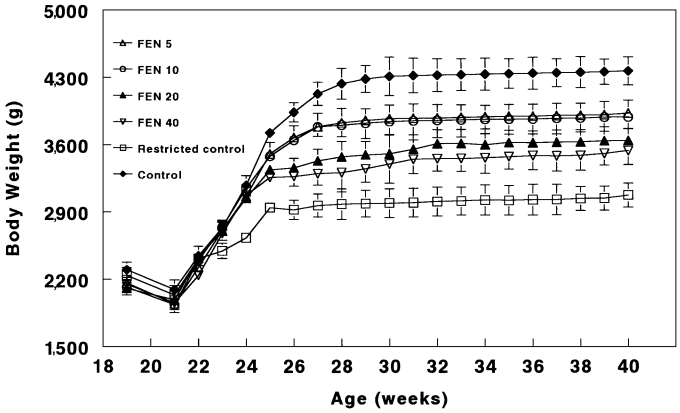

FIGURE 1. Body weights of broiler breeder hens treated with 5 (FEN 5), 10 (FEN 10), 20 (FEN 20), and 40 (FEN 40) mg DL-fenfluramine/kg BW and fed for *ad libitum* intake (control) or feed restricted (restricted control) (mean ± SEM).

Measurements

Individual feed intake (FI) and egg production were recorded daily, and daily average FI and egg laying rate were recorded weekly for each bird. The birds were weighed weekly. Eggs were individually weighed, and their shell, albumen, and yolk were weighed separately. At 40 wk of age, pullets were weighed and killed by cervical dislocation; adipose tissue and ovary were removed and cleared from adhering tissues and weighed.

Statistical Analysis

Data were analyzed by using repeated measurement analysis for BW, FI, and egg production and a one-way analysis of variance for autopsy results using SAS software (SAS Institute, 1996).

RESULTS

Body weights are presented in Figure 1. Administration of fenfluramine depressed ($P < 0.05$) BW in a dose-dependent manner (correlation of –0.65; $P < 0.05$), relative to the control group, but was less effective in this respect than feed restriction.

Feed intake was significantly reduced in a dose-dependent manner in all treated birds (correlation –0.80; $P < 0.05$) (Figure 2). Feeding suppression occurred in two distinct phases; the first lasted 4 wk, during which FI declined progressively. This phase coincided with the period of rapid growth (Figure 1); during the second phase, FI reached a plateau at a significantly low level until the end of the experimental period. The most severe reduction in FI was observed in the FEN 40 group in which, during the second phase, FI was less than 50% of that of the control group.

Peak egg production (Figure 3) was 81.2% at 32 wk, 82.5% at 32 wk, 85% at 33 wk, and 85.5% at 33 wk in the FEN 5, 10, 20, and 40 groups, respectively. *Ad libitum* feeding caused an early initiation of egg production,

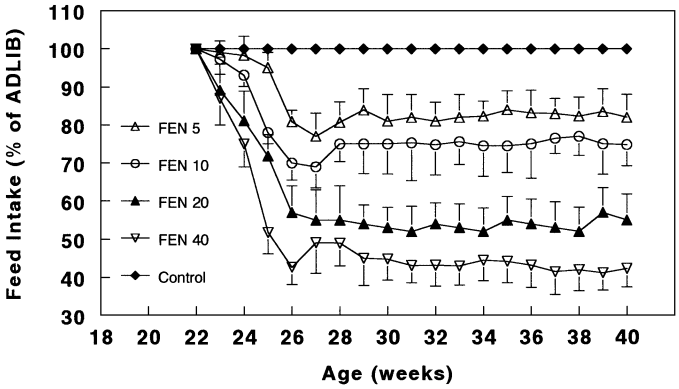

FIGURE 2. Feed intake as a percentage of control (ADLIB; *ad libitum* feeding) of broiler breeder hens treated with 5 (FEN 5), 10 (FEN 10), 20 (FEN 20), and 40 (FEN 40) mg fenfluramine/kg BW and fed for *ad libitum* intake (control) (mean ± SEM; significance is described in the results section).

peaking (81%) at 29 wk of age, followed by a sharp decline in laying rate to a level of 57% at the end of the experimental period. Hens under feed restriction reached peak laying (84%) at 33 wk of age. There were no differences in egg and egg component weights among the treated groups.

A significant dose-related reduction in abdominal adipose tissue weight (Figure 4, a and b) was observed at 40 wk of age in all fenfluramine-treated groups, reaching the lowest levels in the FEN 40 group, similar to values found in the restricted control group. Ovarian weight (Figure 5a) was significantly higher in the restricted control and FEN 40 groups relative to the control and FEN 5 and 10 groups. Similar results, with the exception of the FEN 10 group, were detected when data were tested as a percentage of BW (Figure 5b).

DISCUSSION

The present study demonstrates that, in broiler breeder hens, oral administration of DL-fenfluramine signifi-

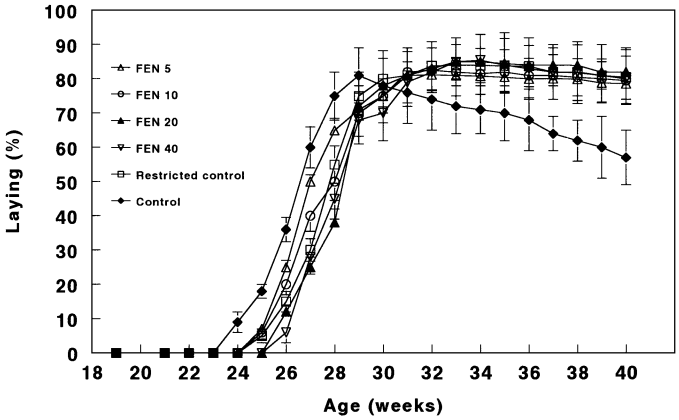

FIGURE 3. Egg production presented as a percentage of laying in broiler breeder hens treated with 5 (FEN 5), 10 (FEN 10), 20 (FEN 20), and 40 (FEN 40) mg fenfluramine/kg BW and fed for *ad libitum* intake (control) or feed restricted (restricted control) (mean ± SEM).

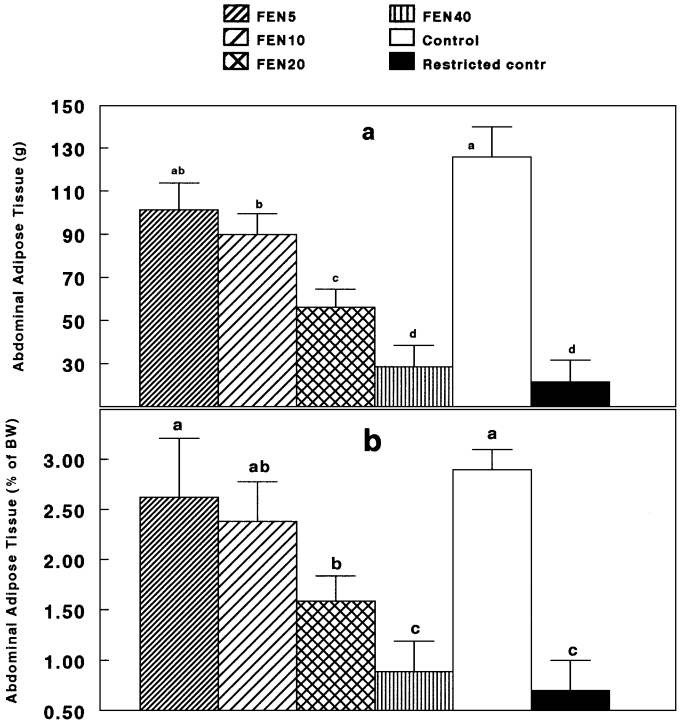

FIGURE 4. Abdominal adipose tissue weight in absolute (a) and relative to BW (b) values of broiler breeder hens treated with 5 (FEN 5), 10 (FEN 10), 20 (FEN 20), and 40 (FEN 40) mg fenfluramine/kg BW and fed for *ad libitum* intake (control) or feed restricted (restricted control) (mean ± SEM). [a–c]Values marked with different letters are different at ($P < 0.05$).

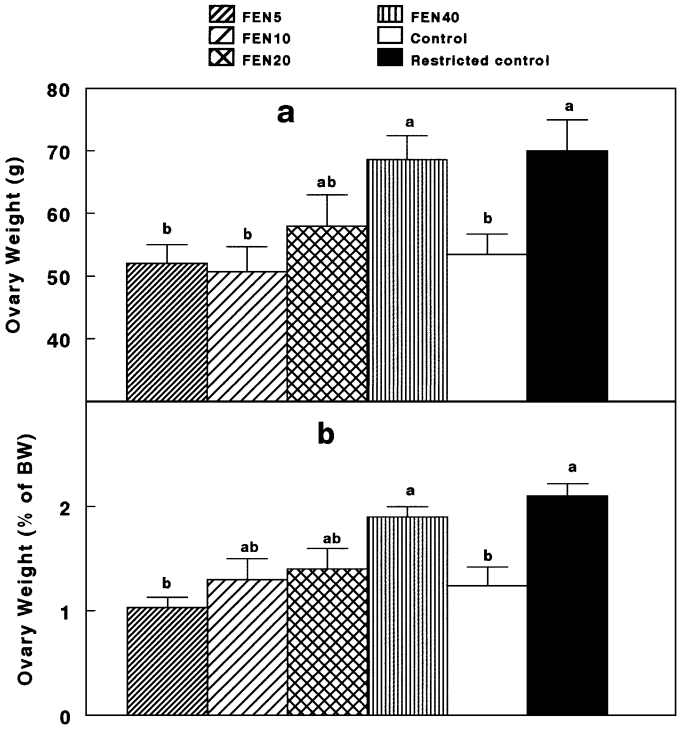

FIGURE 5. Ovarian weight in absolute (a) and relative to BW (b) values of broiler breeder hens treated with 5 (FEN 5), 10 (FEN 10), 20 (FEN 20), and 40 (FEN 40) mg fenfluramine/kg BW and fed for *ad libitum* intake (control) or feed restricted (restricted control) (mean ± SEM). [a,b]Values marked with different letters are different ($P < 0.05$).

cantly reduces FI, BW, and abdominal adipose tissue weight in a dose-dependent manner and has no adverse effect on egg production rate relative to manual feed restriction. These data suggest that DL-fenfluramine can be used as an anorectic agent for chemical feed restriction to prevent fattiness and to maintain low and constant BW in genetically selected heavy birds. Because chemical feed restriction is free of the adverse effects of manual feed restriction, it may even be the preferred method, but the effect of this treatment on egg fertility remains to be assayed.

The reduction in BW and fattiness caused by fenfluramine might be the result of both FI suppression and increased energy expenditure (Pinder *et al.*, 1975; MacLeod *et al.*, 1992; MacLeod and Watson, 1993). Fattiness is known to reduce reproductive capacity in broiler breeder hens. Accordingly, reductions in fattiness *via* either feed restriction or the highest dose of fenfluramine (FEN 40) resulted in significantly higher ovarian weights. A tendency toward ovarian enlargement was also observed in the FEN 10 and 20 groups, but not in the FEN 5 hens. Whereas *ad libitum* feeding resulted in an early peak in egg production followed by a rapid decline in laying rate, the laying patterns were very similar between the feed-restricted hens and those provided with fenfluramine at all given doses. This result suggests that the effect of fenfluramine on laying rate is not correlated with its leaning effect and may be only partially linked to reduced fattiness.

D-Fenfluramine is known to increase the level of 5-HT in the hypothalamus; accordingly, its anorectic effect can be blocked with the serotonin receptor antagonist, metergoline (Garattini *et al.*, 1987). However, a rise in 5-HT in the hypothalamus stimulates prolactin secretion in turkeys (El Halawani *et al.*, 1988) and chickens (Sharp *et al.*, 1984). Prolactin has gonadostatic activity and suppresses egg laying (Rozenboim *et al.*, 1993). Furthermore, DF has been shown to enhance prolactin secretion in rats and humans (Baumann *et al.*, 1998, Young *et al.*, 1998).

However, in the present study, birds were provided with a racimer mixture of DL-fenfluramine. D-Fenfluramine is much more potent than L-fenfluramine in increasing the brain level of 5-HT (Invernizzi *et al.*, 1986). On the other hand, L-fenfluramine has functions that DF does not. It has been found to alter dopamine (Invernizzi *et al.*, 1989) and noradrenaline metabolism (Calderini *et al.*, 1975; Invernizzi *et al.*, 1986) and to enhance acetylcholine secretion in the brain (Invernizzi *et al.*, 1989).

The enhanced egg laying induced by DL-fenfluramine may not be purely the result of a reduction in fattiness; it may also result from alterations in brain catecholaminergic and cholinergic functions.

Fenfluramine is expensive, and, to reduce the cost of this treatment, we highly suggest conducting further studies that will assay the effect of pure racimers of DF and L-fenfluramine on FI, fattiness, and gonadal axis activities in chickens.

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