Effects of Biogenic Amines on Growth and the Incidence of Proventricular Lesions in Broiler Chickens[1]

D. M. Barnes,[2,3] Y. K. Kirby, and K. G. Oliver

Department of Poultry Science, University of Arkansas, Fayetteville, Arkansas 72701

ABSTRACT Biogenic amines have been implicated in a malabsorption syndrome characterized by decreases in feed efficiency and enlargement of the proventriculus. Two studies were conducted to determine the effects of two common biogenic amines, histamine (HIS) and cadaverine (CAD), on broiler growth and the incidence of pathologies associated with proventriculitis. In the first experiment, broiler chicks were fed diets containing 0, 0.01, 0.05, 0.1, and 0.2% HIS, and in the second experiment chicks were fed diets containing 0, 0.1, and 0.2% HIS, 0.1% CAD, or a combination of 0.1% HIS and 0.1% CAD. Histamine at 0.1 and 0.2% or the combination of HIS and CAD (0.1% each) reduced body weight and feed conversion at 21 d of age. Histamine (0.2%) or the combination of 0.1% HIS and 0.1% CAD increased the circumference of the gastric isthmus 14 and 16%, respectively, and the relative weight of the proventriculus by 21 and 36%, respectively. Histamine and CAD increased the total number, incidence, and severity of gizzard erosion and proventricular ulcers (plaques), and decreased the prominence of gastric papillae by 9 to 108%, depending on the lesion and level of biogenic amine. Dietary HIS (0.2%) increased putrescine by 91% and spermidine by 41% in proventriculus, and dietary CAD increased tissue CAD to detectable levels. Analysis of 49 commercially available, animal by-product feedstuffs suggests that if biogenic amines were the singular cause of proventriculitis, the current industry levels of dietary animal protein (5 to 10%) would not compromise growth performance.

(*Key words*: biogenic amine, broiler, histamine, cadaverine, proventriculitus)

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INTRODUCTION

An important, recurrent problem facing poultry integrators is the incidence of proventricular lesions, proventricular enlargement, and other pathologies associated with proventriculitis (Bayyari et al., 1995). These pathologies can result in decreased feed efficiency, decreased weight gain, and increased carcass contamination from gastrointestinal rupture during processing. Similar conditions have been observed that have been attributed to a number of agents, including biogenic amines (Newberne et al., 1956; Poole, 1994) mycotoxins (Pegram and Wyatt, 1981), copper sulfate (Wideman et al., 1995), and an unidentified, filterable infectious agent (Bayyari et al., 1995).

Biogenic amines (histamine, cadaverine, putrescine, spermine, and spermidine) formed by microbial decarboxylation of amino acids are present in many animal protein products. Despite the importance of biogenic amines in normal physiological function and potential involvement in pathological conditions (Pegg, 1986; Wolfe and Soll, 1988), our knowledge of their effects in poultry gastrointestinal tissue is limited. In poultry, biogenic amines have been shown to decrease feed efficiency (Brugh and Wilson, 1986; Stuart et al., 1986) and to induce proventricular enlargement (Shifrine et al., 1960, Harry et al., 1975). In contrast, Smith (1990) has shown enhanced growth in animals fed purified diets fortified with putrescine. Colnago and Jensen (1992), however, failed to observe such a benefit under similar conditions. These data indicate that, although biogenic amines can elicit many of the symptoms of proventriculitis, it is unlikely that they are solely responsible for the pathology.

In addition to the limited performance data, few studies have examined the potential interactions among biogenic amines. The ability of these amines to work synergistically to alter metabolism (Lyons et al., 1983; Bjeldanes et al., 1979) suggests that the total level of biogenic amines may be more important than the level of any single amine. Thus, the objective of the present study was to examine several levels of dietary histamine (HIS) and cadaverine

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[2]To whom correspondence should be addressed: barnes@calshp.cals.wisc.edu.

[3]Current address: Department of Animal Science, University of Wisconsin-Madison, 1675 Observatory Dr., Madison, WI 53706.

Abbreviation Key: CAD = cadaverine; HIS = histamine; PVG = proventriculus + gizzard.

TABLE 1. Composition of basal diet

Ingredient	(g/kg)
Yellow corn	536.0
Soybean meal (48%)	369.8
Poultry oil	51.5
Dicalcium phosphate	16.9
Limestone	13.0
Vitamin premix[1]	5.0
Salt	4.4
Alimet 88%	2.4
Trace mineral mix[2]	1.0

[1]Provided per kilogram of diet: vitamin A, 7,709 IU; cholecalciferol, 2,202 IU; vitamin E, 11 IU; vitamin B_{12}, 0.013 mg; riboflavin, 6 mg; pantothenic acid, 10 mg; choline, 495 mg; vitamin K, 1.5 mg; thiamin, 0.55 mg; niacin, 38 mg; pyridoxine, 1.1 mg; folic acid, 0.8 mg; biotin, 0.055 mg; ethoxyquin, 125 mg; Se, 0.1 mg.

[2]Provided per kilogram of diet: $MnSO_4 \cdot H_2O$, 100 mg; $ZnSO_4 \cdot 7H_2O$, 100 mg; $FeSO_4 \cdot 7H_2O$, 50 mg; $CuSO_4 \cdot 5H_2O$, 10 mg; $Ca(IO_3)_2 \cdot H_2O$, 1 mg.

(CAD), singly or in combination, and determine the incidence of proventricular lesions associated with proventriculitis and the impact on broiler growth. Levels of biogenic amines and their effects in these trials are compared with levels in poultry feedstuffs.

MATERIALS AND METHODS

Animals and Diets

Two experiments were conducted with male broiler chicks (Cobb 500) obtained at 1 d of age from a commercial hatchery. Chicks were housed in heated brooder batteries with raised wire floors and continuous illumination. The chicks were selected to minimize differences in initial body weight (±10% mean flock weight) and were randomly assigned to treatments. Ten chicks were assigned to each pen, and each dietary treatment was replicated with three (Experiment 2) or four (Experiment 1) pens. In the first experiment we tested a range of HIS levels to determine suitable levels to examine in Experiment 2. Appropriate amounts of HIS·HCl[4] to achieve final dietary levels of 0, 0.01, 0.05, 0.10, or 0.20% were mixed in 500 mL of corn oil and added to aliquots of a corn-soybean meal--based diet (Table 1).

Diets were formulated to meet or exceed dietary requirements recommended by the NRC (1994), and chicks were allowed access to feed and tap water ad libitum. Experiment 2 was of similar design except that HIS·HCl was added at 0.1 or 0.2% of the diet (0.1% HIS, 0.2% HIS), CAD[4] at 0.1% (0.1% CAD), and HIS and CAD together at 0.1% each (0.1% HIS/CAD). Amines were prepared in 1.0 L of water and sprayed on allotments of the basal diet. For both experiments, birds and feed were weighed weekly to determine body weight gain and feed consumption. The University of Arkansas Institutional Animal Use and Care Committee approved all experimental protocols.

Experiment 1

Chicks were killed by cervical dislocation at 21 d and the proventriculus and gizzard (PVG) were removed, washed of feed contents, blotted dry, and weighed. Proventriculi from control and 0.2% HIS-treated chickens were further analyzed for their resistance to puncture. Longitudinal sheer strength (a measure of relative resistance to puncture) was determined for 10 untreated birds and 10 birds from the 0.2% HIS treatment by using an Instron Model 4502 shear press.[5] An approximately 4.8 cm^2 (0.75 $inch^2$) section of proventriculus was placed in the shear press, and the peak force (kg) required to puncture the tissue was measured.

Experiment 2

Tissues were obtained at 21 d as described above, and the PVG was scored for lesions previously described for proventriculitis (Bayyari et al., 1995). In addition, the circumference of the gastric isthmus was measured. Proventriculi were evaluated for the appearance and severity of plaques and the prominence of gastric papillae. Lesion scores of 1 to 4 were given for each proventriculus, where 1 represented a normal proventriculus and 4 represented extensive plaque formation or severe flattening of the gastric papillae. The gizzard lining was scored for evidence of erosion and discoloration on a scale of 1 to 4. Tissues were frozen at –20 C until analyzed for biogenic amines. Analysis for biogenic amines was as previously described (Eerola et al., 1993). Briefly, 2 g of proventriculus was homogenized in 0.4 *M* perchloric acid, containing hexamethylene diamine as an internal standard, with a tissue homogenizer.[6] Aliquots of the supernatant were derivatized with dansyl chloride,[7] and the conjugated amines were separated on a C18 reverse phase column[8] with a 0.1 *M* ammonium acetate:acetonitrile gradient at 1.0 mL/min. Amines were detected by fluorescence (excitation: 335 nm; emission: 515 nm).

Statistical Analysis

Data from both experiments were analyzed using the general linear models procedure of SAS® software (SAS Institute, 1985). Differences among scored data means were analyzed using PROC NPar1way with the Wilcoxon option (Sokal and Rohlf, 1995). All other differences among treatments were separated using Tukey's test or contrasts where appropriate.

RESULTS

Experiment 1

Data for 21-d body weight, feed conversion ratio (FCR), and weight of the combined PVG are presented in Table

[4]Sigma, St. Louis, MO 63178.
[5]Instron Model 4502, Instron Corp., Canton, MA 02021.
[6]Model GLH, Omni International, Warrenton, VA 20187.
[7]Pierce Chemical Co., Rockford, IL 61105.
[8]Nova-Pak, Waters Corp., Milford, MA 01757.

TABLE 2. Growth performance and the combined weight of the proventriculus and gizzard (PVG) of chicks fed diets containing the indicated levels of histamine hydrochloride (Experiment 1)

Dietary treatments	BW[1] (21 d)	Feed:gain	PVG[2] (g)	PVG/BW (% BW)
Basal	725 ± 6[a]	1.62 ± 0.04[c]	27.3 ± 0.9	3.8 ± 0.02[b]
0.01% histamine	725 ± 9[a]	1.68 ± 0.04[bc]	28.1 ± 1.2	3.9 ± 0.05[b]
0.05% histamine	714 ± 23[ab]	1.75 ± 0.03[ab]	26.0 ± 0.8	3.6 ± 0.10[b]
0.10% histamine	680 ± 7[bc]	1.69 ± 0.04[bc]	25.2 ± 0.6	3.7 ± 0.11[b]
0.20% histamine	658 ± 7[c]	1.76 ± 0.06[ab]	28.3 ± 0.9	4.7 ± 0.32[a]

[a–c]Means within columns with no common superscript differ significantly ($P < 0.05$).

[1]Values represent means ± SEM, n = 4.

[2]n = 40.

2. Body weight was significantly reduced by dietary addition of 0.1 and 0.2% HIS (6.2 and 9.2%, respectively), and FCR was decreased by addition of 0.05 or 0.2% HIS. PVG weights were unaffected by increasing levels of HIS; however, when expressed as a percentage of total body weight, 0.2% HIS increased the relative weights compared with those of basal chickens. Feed intake was not affected by any treatment (data not shown). There were also no differences between the shear strengths of proventriculi from basal birds and those consuming 0.2% HIS (37.2 ± 2.5 and 39.6 ± 2.4 kg, respectively).

Experiment 2

Data for 21-d body weight, FCR, weights of the proventriculus, and the combined PVG are presented in Table 3. Body weight was significantly reduced by the dietary addition of 0.1% HIS/CAD and 0.2% HIS (6.1 and 13%, respectively) but not at 0.1% of either amine alone (Table 3). As in Experiment 1, the effects of the amines on the PVG were not observed as gross changes in organ size. However, when the combined PVG weight was expressed as a percentage of body weight, it was significantly increased by 0.2% HIS in the diet. In addition, the weight of the proventriculus alone, expressed as a percentage of body weight, was significantly increased with 0.1% HIS/CAD or 0.2% HIS in the diet. The circumference of the gastric isthmus, a measure of proventricular dilation, was significantly increased in the birds treated with 0.1% HIS/CAD or 0.2% HIS.

Proventriculitus has been characterized by several lesions associated with the upper digestive tract including erosion of the gizzard lining, formation of plaques in the proventriculus, and loss of papillae prominence in the proventriculus (Bayyari et al., 1995). The effects of dietary biogenic amines on these lesions are shown in Table 4. Higher lesion scores and greater incidence of lesions were consistently observed for the highest levels of dietary amine supplementation (0.1% HIS/CAD, 0.2% HIS) compared with the basal diet. Gizzard lining erosion was also significant in birds fed the 0.1% HIS diet compared to control birds (Table 4).

Because several proposed mechanisms of amine action involve intracellular targets, we measured the levels of biogenic amines in the tissue. Measurements of biogenic amine concentration in the proventriculus are presented in Table 5. Dietary addition of HIS did not significantly increase the levels of HIS, CAD, or spermine found in the proventriculus. Spermidine levels in the proventriculus were higher in birds fed the 0.2% HIS treatment than all other treatment groups ($P < 0.05$). In contrast, CAD was only detected in proventriculi obtained from the CAD-treated chickens. Dietary HIS, and not CAD, also increased tissue levels of putrescine. Dietary CAD alone increased tissue HIS levels but not when fed in combination with HIS.

Biogenic Amines in Poultry Feedstuffs

Table 6 details the levels of biogenic amines of 49 commercial feeds or feedstuffs submitted to the University

TABLE 3. Effects of dietary biogenic amines on growth performance, combined proventriculus and gizzard weight (PVG), proventriculus (PV) weight, and the circumference of the gastric isthmus of chicks fed diets containing the indicated levels of biogenic amines (Experiment 2)[1]

Treatment[2]	BW[3] (g)	Feed:gain	PVG (g)	PV (g)	PVG/BW (% BW)	PV/BW (% BW)	Gastric isthmus circumference (mm)
Basal	797 ± 17[a]	1.40 ± 0.05[b]	22.6 ± 0.7	5.0 ± 0.2	2.84 ± 0.08[b]	0.60 ± 0.03[c]	30.3 ± 1.0[b]
0.1% HIS	761 ± 13[ab]	1.47 ± 0.03[b]	21.0 ± 0.4	5.1 ± 0.2	2.78 ± 0.07[b]	0.67 ± 0.02[bc]	31.7 ± 1.3[ab]
0.1% CAD	807 ± 15[a]	1.36 ± 0.01[b]	22.0 ± 0.7	5.2 ± 0.3	2.73 ± 0.08[b]	0.63 ± 0.04[bc]	33.2 ± 1.8[ab]
0.1% HIS/CAD	748 ± 15[b]	1.49 ± 0.03[b]	21.4 ± 0.6	5.3 ± 0.4	2.87 ± 0.07[b]	0.73 ± 0.05[ab]	34.5 ± 2.0[a]
0.2% HIS	693 ± 15[c]	1.66 ± 0.06[a]	22.1 ± 0.5	5.6 ± 0.2	3.22 ± 0.08[a]	0.82 ± 0.05[a]	35.3 ± 1.4[a]

[a–c]Means within columns with no common superscript differ significantly ($P < 0.05$).

[1]PVG and PV weights are also reported as a percentage of BW.

[2]CAD = cadaverine; HIS = histamine.

[3]Values represent the mean ± SEM of 15 birds.

TABLE 4. Effects of dietary histamine (HIS) and cadaverine (CAD) on lesions of the proventriculus and gizzard

Treatment	Organ[1,2]			Total lesions[3]
	Papillae	Plaques	Gizzard lining	
Basal	1.2 ± 0.1[b]	1.1 ± 0.1[b]	1.2 ± 0.1[c]	6
0.1% HIS	1.5 ± 0.2[ab]	1.3 ± 0.1[ab]	1.8 ± 0.2[b]	18
0.1% CAD	1.4 ± 0.2[ab]	1.2 ± 0.1[ab]	1.5 ± 0.2[bc]	11
0.1% HIS/CAD	2.0 ± 0.3[a]	1.5 ± 0.2[a]	1.7 ± 0.2[b]	22
0.2% HIS	1.8 ± 0.2[a]	1.5 ± 0.2[a]	2.5 ± 0.2[a]	26

[a–c]Means within columns with no common superscript differ significantly ($P < 0.05$).

[1]Organs were given a score of 1 (normal), 2 (mild lesions), 3 (moderate lesions), or 4 (severe lesions) based on the severity of the lesions as described in the text. Papillae were judged on their prominence, plaques were judged based on their number and size, and gizzard erosion was judged on the number and size of the lesions.

[2]Values represent the mean ± SEM of 15 birds.

[3]Values represent the number of observations scored 2 or greater for 15 birds.

of Arkansas Central Analytical Laboratory for analysis. Samples were submitted over the course of a year and grouped into categories based on customer description. Data are presented as the median value (mg/kg) for each biogenic amine and the range observed for all samples in a category. Putrescine, spermine, and CAD were highest in poultry meal; histamine and spermine were highest in fish meal.

DISCUSSION

Biogenic amines have been implicated in a malabsorption syndrome (proventriculitis or proventricular hyperplasia) characterized by decreases in feed conversion and enlargement of the proventriculus (Stuart et al., 1986). The effects of biogenic amines, specifically HIS, on the enlargement of the proventriculus and decreased body weight have long been known (Newberne et al., 1956). However, based on earlier studies, the interactions of dietary amines and physiology are complex. For example, Bjeldanes et al. (1979) reported an additive effect from co-addition of CAD and putrescine on broiler growth, whereas Bermudez and Firman (1998) reported no effect on broiler growth for a mixture containing HIS, CAD, putrescine, and phenylethylamine added to the diet. The physiological and biochemical basis for the interactions between biogenic amines are poorly understood in birds; however, extensive research has been conducted in rodents. In rat intestine, CAD has been shown to increase cellular uptake of HIS (Lyons et al., 1983) and to decrease the activity of amine oxidase, an important HIS-metabolizing enzyme (Taylor and Lieber, 1979). Thus, CAD could enhance the actions of low levels of HIS, an hypothesis supported by Stuart et al. (1986) and suggested by the data in Tables 3, 4, and 5.

Histamine that is injected or obtained from dietary sources increases gastric acid secretion and causes enlargement of the proventriculus (Newberne et al., 1956; Shifrine et al., 1960; Harry et al., 1975). The depression in body weight, increased feed conversion, and increased proventricular lesions observed in the present study concur with previous reports. Shifrine et al. (1960) fed 0.25, 0.5, and 1.0% HIS and found a dose-dependent decrease in body weight and feed consumption and an increase in the incidence of proventricular enlargement.

Harry et al. (1975) and Stuart et al. (1986) fed 0.1 to 1.0% and 0.06 to 0.26% HIS, respectively, and observed similar effects. In contrast, Brugh and Wilson (1986) fed 0.2% HIS and reported a low incidence of proventricular enlargement. Stuart et al. (1986) have performed the most comprehensive pathological study on the effects of different biogenic amines and demonstrated that biogenic amines (HIS, CAD, or putrescine) alone or in combination with mycotoxin T-2 could induce clinical pathologies similar to those observed for malabsorption syndrome. The data reported here support this previous work and dem-

TABLE 5. Effects of dietary histamine (HIS) and cadaverine (CAD) on the levels of amines found in the proventriculus

Treatment	Biogenic amine[1] (mg/kg)				
	Putrescine	Cadaverine	Histamine	Spermidine	Spermine
Basal	7.2 ± 0.3[b]	ND[2]	13.4 ± 1.0[abc]	92.8 ± 4.9[bc]	245 ± 10
0.1% HIS	10.7 ± 1.2[b]	ND	9.7 ± 1.1[a]	90.9 ± 4.6[c]	262 ± 13
0.1% CAD	7.4 ± 0.7[b]	6.8 ± 1.3	17.0 ± 1.7[c]	87.9 ± 4.0[c]	268 ± 21
0.1% HIS/CAD	9.4 ± 0.8[b]	6.4 ± 1.2	13.0 ± 1.6[ab]	108.5 ± 2.7[b]	229 ± 10
0.2% HIS	13.8 ± 1.0[a]	ND	15.7 ± 1.1[bc]	137.3 ± 5.8[a]	224 ± 7

[a–c]Means within columns with no common superscript differ significantly ($P < 0.05$).

[1]Values represent the mean ± SEM of tissues from 15 birds.

[2]ND = not detected.

TABLE 6. Levels of biogenic amines in various animal by-products submitted to the University of Arkansas for analysis

By-product	Biogenic amine[1] (mg/kg)				
	Putrescine	Cadaverine	Histamine	Spermidine	Spermine
Unidentified[2] (n = 19)	21 (ND[3]–618)[4]	38 (ND–860)	49 (ND–3,732)	23 (ND–123)	39 (9–53)
Meat and bone meal (n = 16)	57 (ND–286)	120 (ND–450)	21 (ND–208)	16 (ND–39)	31 (10–56)
Fish meal (n = 9)	99 (12–537)	215 (64–557)	70 (8–1,576)	31 (18–97)	27 (120–139)
Poultry meal (n = 5)	227 (84–390)	451 (140–879)	39 (28–95)	31 (19–53)	74 (55–96)

[1]Median milligrams per kilogram for each amine.

[2]Poultry feedstuffs submitted without reference to composition.

[3]ND = not detected.

[4]Range for samples analyzed.

onstrate that HIS and CAD alone and in combination can induce many of the pathologies associated with proventriculitis.

The potential effect of biogenic amines on proventriculus size and dilation of the gastric isthmus are of particular interest, as they represent a potential mechanism by which amines alter feed conversion. The majority of experiments indicate that proventriculus enlargement and dilation can be induced by oral HIS (Newberne et al., 1956; Shifrine et al., 1960; Harry et al., 1975). Indeed, we found significant increases in proventriculus size (relative to BW) and dilation of the gastric isthmus in birds fed 0.2% HIS or 0.1% each of HIS and CAD (Table 3). The change in relative proventriculus size was primarily due to a decrease in body weight; however, the trend was for increasing levels of biogenic amines to increase proventriculus weight. Both experiments showed no differences among treatments of PVG weight. Because these experiments only examined early growth, it may be possible that significant differences in proventriculus and PVG weight would be observed with older birds or longer feeding of the biogenic amines.

Enlargement of the proventriculus and weakening of the gastric isthmus may increase the incidence of gastrointestinal rupture, from longitudinal tears and PVG separation, during evisceration (Bayyari et al. 1995). Measurement of the resistance of the proventriculus to longitudinal tears or punctures in Experiment 1 indicated that at 3 wk there was no difference between control and HIS-treated chickens. Although dilation of the gastric isthmus was not measured in this experiment, observations from Experiment 2 with similar levels of HIS suggest that significant increases in dilation could be expected. The action of HIS on proventriculus enlargement and gut fragility is possibly due to its effects on gut motility and acid secretion. High levels of HIS attenuate gut contractions (Matsunaga et al., 1994; Jennings et al., 1995) and could result in a flaccid dilated proventriculus.

Histamine also acts to stimulate gastric acid secretion from the parietal cell through the H2 receptor, and, if dietary HIS exceeds the capacity for degradation, it may result in continuous stimulation of gastric acid secretion (Obrink, 1991). The increased and sustained acid secretion could lead to erosion of the distal gastrointestinal tract as reported in Table 4. Erosion of the gizzard lining, characterized by discoloration and ulceration, has been observed with high levels of HIS (Harry et al., 1975). In addition Stuart et al. (1986) describe lesions in the small intestine that may be due to excessive acid secretion associated with the presence of dietary biogenic amines.

Another lesion associated with proventriculitis is the formation of white plaques in the proventriculus mucosa. These whitish plaques are characterized by mild to moderate infiltration of lymphocytes (Stuart et al., 1986) and a milky exudate when lanced (Bayyari et al., 1995). It does not appear that excessive HIS in tissue caused cellular damage and infiltration of lymphocytes because dietary HIS did not significantly increase HIS levels in tissue (Table 5). The HIS-metabolizing enzymes (diamine oxidase) might have been sufficient to prevent tissue accumulation in birds fed HIS. The levels of HIS metabolites were not determined in this study and thus remain a possible mediator of plaque formation. Gastric acid secretion may also play a role in plaque formation. The hyperstimulation of acid secretion may overwhelm defense mechanisms and lead to localized cellular damage.

Biogenic amines are the decarboxylation products of amino acids typically formed by bacterial decomposition or putrefaction of animal proteins (offal, dead or decaying animals, etc.). Improperly stored raw product and bacterial contamination of product after rendering are the most likely sources of dietary biogenic amines. Previous reports have indicated that CAD, putrescine, and HIS are the amines generally found at the highest levels in animal byproducts (Poole 1994); however, information is limited as to whether the levels found in poultry feeds are capable of inducing proventriculitis (Stuart et al., 1986).

The data presented in Table 6 support previous findings for the presence of biogenic amines in poultry feedstuffs; however, unlike earlier reports, we found that HIS was generally present to the same degree as spermine and spermidine (Table 6). As expected, samples containing fish generally contained the highest levels of HIS; however, their total biogenic amine load (composite mg/kg of all amines) was approximately half of that found in poultry meal (Table 6). Poultry meal was highest in CAD and putrescine. Cadaverine can inhibit HIS degradation, thereby increasing tissue HIS levels. Thus, the high levels of CAD found in poultry meal could lead to effectively higher tissue concentrations of HIS than may

occur with a fish product. The high levels of CAD and putrescine found in poultry meal also suggest that these products undergo more microbial degradation than the meat and bone meal or fish meal products.

Data from Stuart et al. (1986) and this report suggest that in considering the impact of biogenic amines on the pathologies associated with proventriculitis, it may be most appropriate to combine the levels of CAD and HIS present. Calculations of the combined biogenic amine load (HIS + CAD) for fish meal or poultry meal results in 0.028 or 0.049% biogenic amines, respectively. Including these feedstuffs in a diet at 10% would result in approximately 0.003 and 0.005% biogenic amine in the diet. These levels are far below any dose previously reported to induce proventricular enlargement or other related lesions. Even the commercial sample with the highest level of amines (860 mg/kg CAD; 3,742 mg/kg HIS) fed at 10% would have resulted in 0.046% biogenic amine in the diet. This percentage of HIS failed to alter growth parameters in Experiment 1. These data suggest that dietary biogenic amines alone do not cause proventriculitis with commercial diets; however, the interaction among amines and the other causative agents (Cu^{2+}, mycotoxin) remains to be determined. One possible scenario is for two or more of these agents to work synergistically to induce proventriculitis.

In summary, dietary HIS and cadaverine can cause the pathologies associated with proventriculitus; however, only feed ingredients extremely high in these amines are likely to affect growth. The action of HIS and CAD appear to be additive or synergistic, suggesting that the dietary amine load may be a better indicator of potential performance problems associated with dietary biogenic amines.

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