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Influence of a Propionic Acid Feed Additive on Performance of Turkey Poults with Experimentally Induced Poul Enteritis and Mortality Syndrome¹

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ABSTRACT Poul enteritis and mortality syndrome (PEMS) has multiple etiological agents associated with its occurrence, including two viruses and at least three *Escherichia coli* isolates. Myco Curb (MC) contains organic acids and is used as a feed additive to inhibit growth of many bacteria and toxin-producing molds but not viruses. Studies evaluating the influence of MC on BW, feed conversion, and mortality indicate that turkey poults tolerate MC at 1.25% but not 2.50%, but higher MC content in feed provides greater suppression of growth of bacterial isolates commonly associated with PEMS. In two PEMS experiments, 1.25% MC was blended into poul starter feed and was maintained in the feed for the duration of the 3-wk experiments. In these experiments, 1-d-

old commercial poults were placed into battery brooders and were given turkey starter feed and water ad libitum. At 6 d posthatch, PEMS-designated poults were given a 1-mL oral gavage of a 10% suspension of feces from PEMS-infected poults. BW depression due to PEMS was not alleviated by MC, although there was less variation in mean BW of the MC-fed poults, and there was a highly significant reduction in mortality (68% in PEMS-exposed with MC vs. 32.5% in PEMS-exposed without MC). The reduction in mortality in the MC-fed poults was attributed to decreased bacterial content of the gut and to maintenance of packed cell volume and hemoglobin content. It was concluded that MC might be a potential nutritional intervention during PEMS.

(Key words: poul enteritis and mortality syndrome, poul, propionic acid, antibacterial activity, hematology)

2002 Poultry Science 81:951–957

INTRODUCTION

Poul enteritis and mortality syndrome (PEMS) is a term that describes potentially lethal enteritis of young turkeys (Barnes et al., 1996). It is caused by agents such as bacteria and viruses that irritate and injure the intestines (Edens et al., 1997b,c,d; Guy et al., 2000; Heggen et al., 2000; Qureshi et al., 2000; Shultz-Cherry et al., 2000, 2001; Yu et al., 2000a,b).

Immune dysfunction associated with PEMS (Qureshi et al., 1997; Heggen et al., 2000) increases susceptibility to secondary bacterial infection that ultimately will kill poults (Edens et al., 1997b,c,d). Edens et al. (1997b,c,d) consistently isolated from moribund, PEMS-infected poults two atypical strains of *Escherichia coli* (colony type 1 and colony type 2). Furthermore, Edens et al. (1997b,c,d) observed that the *E. coli* strains involved in PEMS were resistant to most of the antibiotics commonly used by

the turkey industry. Therefore, the observation that there were some apparently atypical *E. coli* isolates involved in PEMS represented a significant breakthrough in the diagnosis and control of PEMS.

Because PEMS is a major economic threat to the turkey production sector of the U.S. poultry industry, it is important to explore potential interventions that may ameliorate its severity. The development of PEMS appears to be influenced by *Escherichia coli*, *Salmonellae*, and other *Enterobacteriaceae* (Edens et al., 1997b,c,d). There are at least two atypical *E. coli* along with numerous other untyped *E. coli* involved in the PEMS problem (Edens et al., 1997b,c,d). Additionally there are at least 14 isolates of *Salmonellae* and at least one atypical *Salmonella* that are commonly associated with PEMS, and most of these isolates show a broad range of resistance to antibiotics used by the turkey industry (Edens et al., 1997b,c,d).

There may be interactions among different bacterial pathogens that contribute to PEMS and exacerbate its severity (Edens et al., 1997b,c,d). A single population of pathogenic microbes often can be competitively regulated or excluded by other microbes in the intestinal tract with little negative influence on the performance of the poul

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Received for publication June 4, 2001.

Accepted for publication February 8, 2002.

¹Use of trade names in this article does not imply endorsement by the North Carolina Agricultural Research Service of the product named or criticism of similar products not named.

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Abbreviation Key: Hgb = hemoglobin; MC = Myco Curb; PCV = packed cell volume; PEMS = poul enteritis and mortality syndrome.

(Edens et al., 1997a), but combinations of microbes or feed molds (toxins) may allow proliferation of normally innocuous bacteria that will make the poult more susceptible to disease (Edens et al., 1997a). Environmental conditions, nutrition, and chemotherapeutic chemicals can influence the control of microbial populations and the effects of molds and their toxins in poultry species such as the turkey poult (Edens, 1996; Edens and Doerfler, 1998; Edens et al., 1998).

Therefore, intervention research that addresses the potential use of nonantibiotic substances as a means for amelioration of the detrimental effects of PEMS is important. Myco Curb (MC), a mold inhibitor for processed feed ingredients and animal feeds, contains organic acids (primarily propionic acid) that are effective against various bacteria and fungi (Kemin Industries, 1986, 1993; Pumfrey and Nelson, 1991; Hume et al., 1993; Larson et al., 1993; Huff et al., 1994). Anecdotal information from a turkey producer in Western North Carolina indicated that MC (0.625%) reduced mortality in flocks of poult that were suspected to have developed PEMS (without MC, 12.47%; with MC, 5.52%). Therefore, a product such as MC appeared to have potential for immediate use as a nutritional intervention in PEMS.

MATERIALS AND METHODS

Animal Welfare

This project was approved and conducted under the supervision of the North Carolina State University Animal Care and Use Committee, which has adopted Animal Care and Use Guidelines governing all animal use in experimental procedures.

Poult and Husbandry

British United Turkey poult were obtained and transported from a commercial hatchery to North Carolina State University. These 1-d-old poult were wing-banded, weighed, and placed, in groups of 10, into pens in Petersime³ heated battery brooders where water and turkey starter feed (North Carolina Agricultural Research Service; metabolizable energy: 2,915 kcal/kg; crude protein: 28.13%) with or without MC were provided ad libitum. The poult were not subjected to hatchery services such as beak or toe trimming, antibiotic administration, or vaccinations. Continuous lighting was provided by incandescent lamps in the ceiling of each room. Two experiments were conducted. The first was a dose titration study to determine an adequate level of MC that would maximize the growth and feed conversion of male and female poult, and the second was conducted to determine the influence of MC on performance of PEMS-infected male poult. At the time of placement for Experiment 2, two

groups of poult (controls and those designated for PEMS-exposure) were assigned to separate but identical controlled-environment isolation rooms.

Brooding Temperatures

Ambient temperature for brooding was maintained by room air conditioning using a thermostatically controlled hot/cold water heat exchange system mediated by a forced draft. Initial room brooding temperature for the control and PEMS rooms was set at 34 C, and this temperature was decreased 3 C in each room at 7, 14, and 21 d of brooding. Humidity in the experimental rooms was not controlled and varied from 47 to 63% relative humidity.

Experimental Design

The dose titration experiment used a 2 × 4 × 5 factorially arranged completely randomized statistical design. There were 50 male and 50 female poult in each of four different feed additive treatments. MC⁴ was blended in dry mash diets to provide a dietary concentration of 0, 0.625, 1.25, or 2.50%. There were five replicate pens assigned for each sex and MC dietary treatment. A total of 50 pens with 10 poult per pen were involved. Thus, 500 poult were included in the first experiment, which was conducted over 21 d. Based on the results from Experiment 1, a 1.25% MC addition rate was chosen for use in Experiment 2. The second experiment used a factorially arranged 2 (control vs. PEMS) × 2 (0 vs. 1.25% MC) completely randomized experimental design. The MC was blended in feed as described above. Two trials were conducted utilizing this design involving 300 poult per trial. Poult in groups of 10 each were placed into heated battery brooders. Five replicate pens were used for each treatment control group with or without MC, and there were 10 replicate pens for each PEMS treatment groups with or without MC.

PEMS Exposure

At 6 d posthatch, each poult in the PEMS-exposed groups was given a 1-mL oral gavage of a 10% suspension of feces from Coronavirus-negative PEMS-positive poult maintained at the College of Veterinary Medicine at North Carolina State University. This procedure has been documented to induce in experimental conditions a disease state that was equivalent to field cases of PEMS (Edens et al., 1997b,c).

Measurements

Body weights were taken at placement and at weekly intervals through 21 d of age. Birds that died during each of Weeks 1, 2, or 3 were weighed, and their weight gain was included in calculations of weekly feed conversion ratios. Blood samples were collected on a weekly interval for determination of packed cell volume (PCV) and hemoglobin (Hgb) concentration (Phelps et al., 1987) and the

³Petersime Incubator Company, Gettysburg, OH.

⁴Kemin Industries, Inc., Des Moines, IA.

TABLE 1. Influence of Myco Curb on body weight and feed conversion ratios of normal, 3-wk-old, battery-brooded turkey poults

Myco Curb supplement (%)	Male body weight (g)	Male feed:gain (g:g)	Female body weight (g)	Female feed:gain (g:g)
0	447.8 ± 9.9 ^a	1.62 ^b	414.9 ± 9.0 ^a	1.57 ^b
0.625	452.9 ± 9.7 ^a	1.59 ^b	399.9 ± 8.4 ^{ab}	1.55 ^b
1.250	453.1 ± 9.8 ^a	1.58 ^b	395.9 ± 8.6 ^{ab}	1.57 ^b
2.500	424.4 ± 9.8 ^b	1.77 ^a	380.4 ± 8.9 ^b	1.69 ^a

^{a,b}Within a column, means with unlike superscripts differ significantly ($P < 0.05$).

PEMS-exposed poults with and without MC were compared with the unexposed control poults with and without MC.

Bacteriology

In earlier studies, we had determined that the great majority of the bacterial isolates from PEMS-infected poults were *Enterobacteriaceae* (Edens et al., 1997a,b,c,d). Therefore, in Experiment 1, it was decided to monitor *Enterobacteriaceae* in cecal samples collected from control poults with and without MC in their diets. Poults selected for determination of *Enterobacteriaceae* were 14 d of age, and if they had been PEMS-infected, they would be entering into a phase representing the most severe period of diarrhea that would culminate in mortality. Ceca, weighing about 1 g, were collected and placed in sterile stomacher bags containing 9 mL of tetrathionate⁵ and thoroughly emulsified. The samples were streaked onto differential media with minimal selectivity for *Enterobacteriaceae*, such as MacConkey's agar⁵ with 0.15% bile salts, XLT4 agar,⁵ tryptose soy agar⁵ with 5% sheep blood, and Levine eosin methylene blue (EMB) agar.⁵ All cultures were grown at 37 C for 24 h.

Because colony appearance can be altered by close association with other bacteria, 20 representatives of each selected colony type from each of the five cecal samples per treatment were carefully collected by a straight wire directed at the center of a colony without touching the agar surface. Relative plate growth (4+: extensive/over growth/too many to count, 3+: extensive growth/colonies can be enumerated, 2+: moderate growth/easily enumerated colonies; 1+: only a few colonies per plate; <1+: sporadic appearance of bacterial colonies on the plate) of the different selected colonies was determined by examination of the plates with a magnifier associated with the colony counter. These isolates were then grown anaerobically 24 h at 37 C in brain heart infusion broth⁵ (BHI). Differentiation of tribes and sometimes genus of selected *Enterobacteriaceae* was accomplished by developing biochemical profiles using the BBL Enterotube II System⁶ and the API 20E System⁷ according to manufacturer's

protocols following procedures outlined by Ewing (1986) as reported by Edens et al. (1997c,d).

Analyses of Data

All BW, feed conversion, mortality, and blood component data were subjected to analysis of variance using the general linear models procedure of SAS software (SAS Institute, 1996). Statements of significance are based on $P \leq 0.05$ as a minimum level of significance.

RESULTS

The data for the influence of various doses of MC on performance of male and female turkey poults are presented in Table 1. Male and female poults had a significantly lower BW when they were given 2.5% MC in their feed (Table 1). Furthermore, feed conversion was increased with the 2.5% MC supplementation. However, at 14 d of age, when the poults would be developing severe PEMS-associated diarrhea, the relative growth of selected bacterial species commonly found in association with PEMS was decreased with increasing dietary concentrations of MC (Table 2). Based on the effects of MC on common enteric bacterial species found in conjunction with PEMS (Table 2), as well as feed conversion ratios and male and female poult BW in a dose titration study (Table 1), it was ascertained that the 1.25% MC level would be added to the feed in a second experiment focused on the influence of MC on the development of PEMS.

In the second experiment, at 6 d postplacement, the poults in the PEMS-designated isolation room were challenged via oral gavage. At Day 7, only 24 h after challenge, the PEMS-exposed poults had slightly depressed BW compared to the nonexposed control and MC-treated poults (Figure 1). By 14 d of age, the influence of PEMS exposure on BW was clearly evident and significant (Figure 1). Although the surviving poults were severely stunted at 21 d of age, they were beginning to grow again.

The mean daily mortality indicated that the MC feed additive did not prevent the disease from occurring in the PEMS-exposed poults (Figure 2). However, MC did delay the onset of the initial mortality spike associated with the disease (Figures 2 and 3) and reduced the cumulative mortality by more than one-half (68 vs. 32.5%; Figure 3).

⁵Difco Laboratories, Detroit, MI.

⁶Becton Dickinson Microbiological Systems, Cockysville, MD.

⁷BioMerieux Vitek, Inc., Hazelwood, MO.

TABLE 2. Presence of selected *Enterobacteriaceae* in the ceca of randomly selected, 2-wk-old, control turkey poult given Myco Curb in their feed¹

Treatment	Cecal bacterial	Plate growth ²
Control	<i>Escherichia coli</i> type 1 and O114	2+
	<i>Klebsiella pneumonia</i>	2+
	<i>Citrobacter freundii</i>	1+
	<i>Enterobacter aerogenae</i>	1+
	<i>Serratia fonticola</i>	1+
Myco Curb (0.63%)	<i>E. coli</i> type 1 and O114	2+
	<i>Klebsiella pneumonia</i>	2+
	<i>Citrobacter freundii</i>	1+
	<i>Enterobacter aerogenae</i>	1+
	<i>Serratia fonticola</i>	1+
Myco Curb (1.25%)	<i>E. coli</i> type 1 and O114	1+
	<i>Klebsiella pneumonia</i>	1+
	<i>Citrobacter freundii</i>	<1+
	<i>Enterobacter aerogenae</i>	<1+
	<i>Serratia fonticola</i>	<1+
Myco Curb (2.5%)	<i>E. coli</i> type 1 and O114 ³	<1+

¹N = 5 for each dietary treatment.

²Indicates relative bacterial growth on plates; 4+: extensive/over growth/too many to count, 3+: extensive growth/colonies can be enumerated, 2+: moderate growth/easily enumerated colonies; 1+: only a few colonies per plate; <1+: sporadic appearance of bacterial colonies on the plate.

³These were the only types found in this treatment group.

The PCV of nonexposed control and MC-treated poult did not differ between groups (ranging between 32 and 35%) throughout the experiment (Figure 4). However, the PEMS-exposed poult experienced a rapid increase in PCV that was elevated significantly within 2 d after exposure (Figure 4). The PCV in the PEMS-exposed groups peaked at 45% at 9 d after exposure to the PEMS challenge. From 15 to 19 d of age, PCV in PEMS-exposed poult decreased to the level of the nonexposed control poult. At 11 d of age (5 d postexposure), the PEMS-exposed poult receiving MC in their diet also showed a significant, but transitory, increase in PCV (39%; Figure 4) that was significantly less than the 45% peak in the PEMS-exposed poult not given MC. By 15 d of age, MC-treated PEMS-exposed poult showed a significant

decrease in PCV that returned to nonexposed control levels by 19 d of age (Figure 4).

Blood Hgb responses to PEMS and MC treatment (Figure 5) presented a profile similar to that of PCV (Figure 4). Nonexposed control and MC-treated poult showed Hgb levels between 9 and 10.5 g/dL throughout the trials. However, the blood Hgb levels of PEMS-exposed poult increased immediately by Day 7 (1 d after PEMS exposure) and peaked (14 g/dL) at 15 d of age. From 15 to 17 d of age, Hgb levels decreased significantly to levels comparable to those the nonexposed control and MC-treated groups but continued to show a significant decrease through 19 d of age (Figure 5). The MC-treated PEMS-exposed poult experienced a small but significant increase and peak (11.5 g/dL) in blood Hgb levels 5 d (11 d of age) after exposure (Figure 5). However, by 15

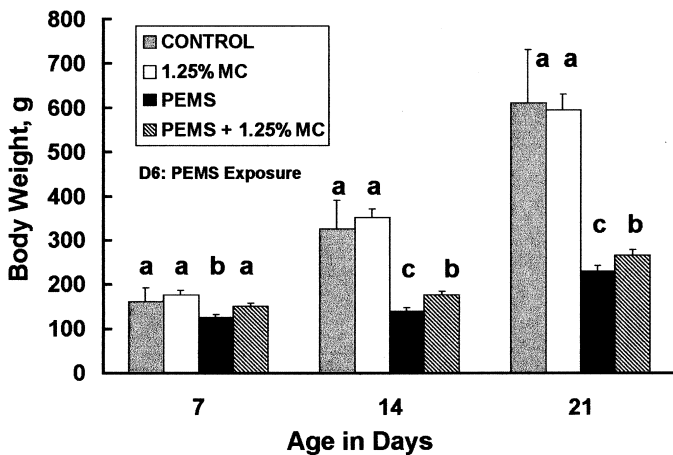


FIGURE 1. Weekly body weights for control, Myco Curb (MC), poult enteritis and mortality syndrome (PEMS), and Myco Curb + PEMS treatment groups. Unlike lowercase letters above the bars of the histograms indicate significant differences among the treatment groups ($P < 0.05$).

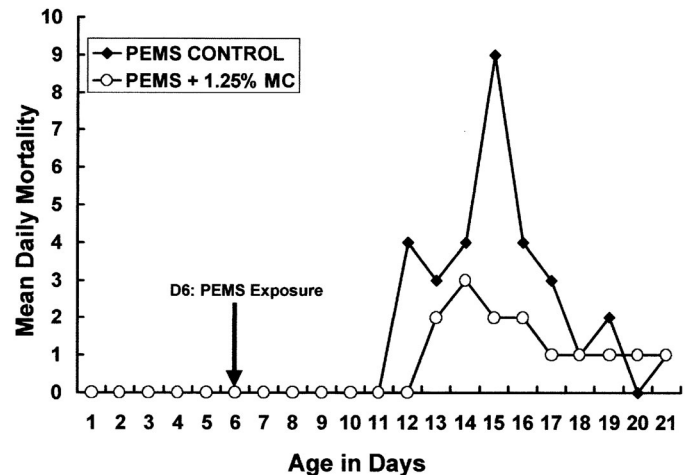


FIGURE 2. Mean daily mortality profile for control, Myco Curb (MC), poult enteritis and mortality syndrome (PEMS), and Myco Curb + PEMS treatment groups. D6 = Day 6.

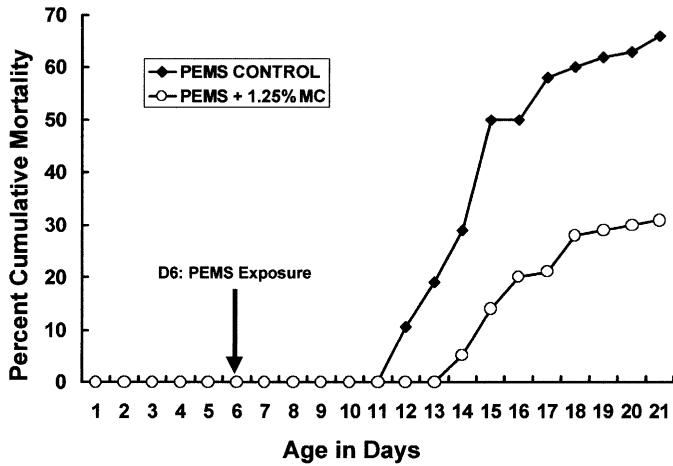


FIGURE 3. Percentage cumulative mortality for control, Myco Curb (MC), poult enteritis and mortality syndrome (PEMS), and Myco Curb + PEMS treatment groups.

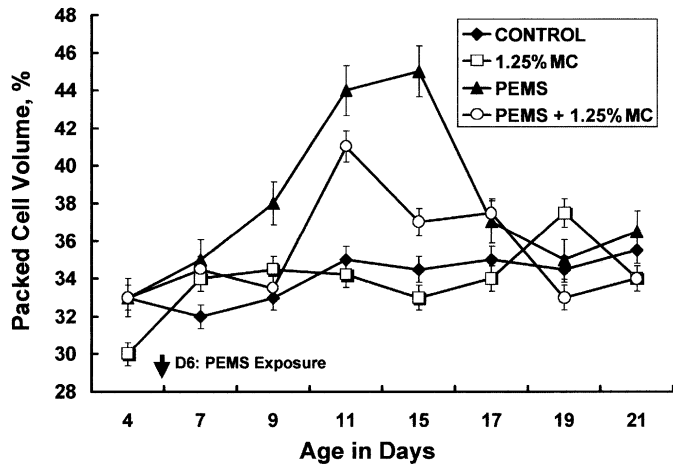


FIGURE 4. Effect of Myco Curb (MC) and poult enteritis and mortality of syndrome (PEMS) on percentages of packed cell volumes.

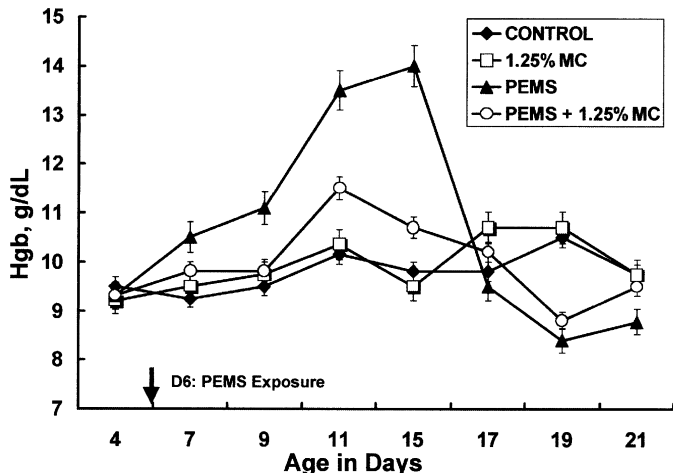


FIGURE 5. Blood hemoglobin responses to poult enteritis and mortality syndrome (PEMS) and Myco Curb (MC) treatments.

d of age the PEMS-exposed MC-treated poult had a lower Hgb level, and by 17 d of age the blood Hgb level had returned to nonexposed control and MC-treated levels. These levels continued to decrease through 19 d of age to a level that was significantly lower than nonexposed Hgb levels (Figure 5). By 21 d of age, all treatment groups, with the exception of the PEMS only group, had similar blood Hgb levels (Figure 5).

DISCUSSION

MC as a feed additive exerts its action primarily via propionic acid, a volatile fatty acid, when in its undissociated lipophilic form easily penetrates bacterial cell walls (Hinton et al., 1990). Once inside the bacterial cell, the acid may dissociate and kill the cell (Hinton et al., 1990). However, the effectiveness of propionic acid to control *Enterobacteriaceae* such as *Salmonellae* appears to depend on the severity of *Salmonellae* challenge (Hume et al., 1993). Additionally, antibacterial properties of propionic acid diminish in the distal end of the intestinal tract as a result of reduced concentrations as it is absorbed, dissociated, and metabolized as a precursor in the tricarboxylic acid (TCA) cycle (Bolton and Dewar, 1964; Hinton et al., 1990; Hume et al., 1993).

Anaerobic bacteria found in the intestinal flora of mature poultry produce volatile fatty acids as a natural mechanism of host resistance to *Salmonellae* infestation (Corrier et al., 1990). However, young birds, especially during the first few days of life, do not have this established flora, and are more susceptible to pathogenic bacterial infections (Corrier et al., 1990), such as those associated with PEMS.

Previous studies have shown that propionic acid probably influences appetite (Cave, 1978) and palatability (Cave, 1984) in chicks. However, when propionic acid is supplemented up to 3% in the diet, no significant effects on feed intake were noted (Fancher and Jensen, 1988). Nevertheless, the data in this study indicated that the addition of 2.50% MC in diets given to young turkeys was not tolerated as well as 3.0% is in chicks. This observation was consistent with that made by Donaldson et al. (1994) who reported decreased feed intake and growth when 2 or 4% propionate salts were given to newly hatched turkey poult.

Brake (Kemin Industries, 1993) indicated that the presence of a mold inhibitor may reduce microbial flora that are competitive with pathogenic bacteria. In one experiment, pathogenic bacteria caused a decrease in mortality in MC-treated (1% MC supplementation) broiler breeders during Weeks 12 to 14 compared to the control birds (Kemin Industries, 1993). Thus, the same phenomenon might occur, which was indicated by the microbiological data from the cecal samples in the first experiment (Table 2): MC at the 1.25 and 2.5% significantly reduced cecal populations of *Enterobacteriaceae* tribes and genera of bacteria. Therefore, a fine line exists between the quantity of feed additive required to reduce pathogenic bacteria and

the quantity that possibly could affect commensal bacterial of the gut.

A systematic investigation to determine the effects of MC on PEMS-infected poult had not been conducted previously. MC fed at the 1.25% level in the diet of PEMS-challenged poult did not prevent the disease from occurring in the PEMS-challenged poult or the growth depression associated with PEMS. However, it did reduce the cumulative mortality by 50% and produced a delay in the onset of the initial mortality spike (Figures 2 and 3). Dietary MC at 1.25% decreases bacterial load in the intestine and ceca. Therefore, it is possible that, at 1.25%, there was a decrease in the pathogenic bacterial load in the intestines or decreased colonization by various *Enterobacteriaceae* in PEMS-infected poult; however, the microbiological influence of MC in PEMS-infected poult was not determined in this study. Nevertheless, there are viruses such as newly identified and characterized turkey Astroviruses (Qureshi et al., 2000, 2002; Shultz-Cherry et al., 2000 and 2001; Yu et al., 2000a,b) that induce a condition comparable to PEMS. It is, perhaps, possible that MC did not have any inhibitory influence on novel viruses associated with PEMS (Qureshi et al., 2000, 2002; Shultz-Cherry et al., 2000 and 2001; Yu et al., 2000a,b; Heggen-Peay et al., 2002), but its antibacterial influence possibly reduced the severity of enteric bacterial loads in PEMS-challenged poult in this study. The reduced bacterial load in control poult (Experiment 1) attributed to MC possibly is reflected in the overall decrease in mortality in MC-treated, PEMS-challenged poult (Experiment 2). However, the severity of the PEMS challenge in this study (1 mL of a 10% suspension of fecal matter from PEMS infected poult) was 10-fold greater than the PEMS challenge given in subsequent studies (0.1 mL of a 10% suspension of fecal matter from PEMS-infected poult) and might have been too large to be effectively suppressed by MC at 1.25%. Additional work with MC and its influence in PEMS appears to be warranted.

Hemoconcentration, as indicated by a PCV of 45% in PEMS-infected poult was maximized 7 to 8 d after exposure. This peak coincided with the period of greatest diarrheal flushing, lack of appetite, dehydration, weight loss, and mortality similar to the observations made by Edens and Doerfler (1998). All of these signs of PEMS disease contribute to reduction in blood volume due to severe dehydration leading to hemoconcentration and increased PCV. At 17 d of age, a more normal PCV developed in PEMS-infected poult. We hypothesized that this was a compensatory response in surviving poult as they attempted to rehydrate themselves.

The results from this study suggested that MC had a positive influence in PEMS-infected poult. The protective effect of MC extended beyond its influence on gut microflora and potential mycotoxins in feeds and to the reduction of the severity of PEMS-related bacterial-induced, but not novel viral-induced, diarrhea that contributed to the hemoconcentration associated with PEMS.

MC may have the potential to be more effective in the field, where poult are subjected to repeated challenges

through bacterial contamination of feed, litter, or drinking water. In those common but hostile environments, where there was increased risk of exposure to overwhelming numbers of potentially pathogenic bacteria, the continuous presence of MC at low levels in the diets of poult at risk for development of PEMS may be sufficient to arrest the development of severe, if not lethal, bacterial enteritis.

Thus, MC might have some beneficial effect in improving the performance of turkey poult at risk for PEMS. Its place in the package of managerial procedures to control PEMS appears to be self-evident even though it was not the panacea that all turkey growers would be seeking. Nevertheless, MC has the ability to reduce significantly the early mortality due to PEMS and affects BW and feed conversions as well. With the growing concern about the prophylactic use of antibiotics, low level incorporation of MC into the feed of turkeys and other species of poultry appears to be a feasible low cost intervention against problems associated with bacterial enteritis.

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