A meta-analysis of the feed intake and growth performance of broiler chickens challenged by bacteria

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ABSTRACT The aim of this meta-analysis was to determine the effect of a bacterial immune challenge (*Clostridium* spp., *Escherichia coli*, and *Salmonella* spp.) on the ADFI, ADG, and nutrient partitioning (maintenance requirements and feed efficiency) of broiler chickens. The database used for the meta-analysis included 65 articles that were published between 1997 and 2012 concerning a total of 86,300 broilers and containing information on the feed intake, protein intake, methionine intake, and weight gain of broilers that were challenged with *Clostridium* spp., *E. coli*, or *Salmonella* spp. and were fed or not fed feed additives. The results of the ADFI and the ADG of the challenged broilers were transformed into values relative to those obtained in control broilers (ΔADG and ΔADFI). The meta-analysis involved 3 sequential analyses: graphical, correlation, and variance-covariance analysis. The results obtained for the birds that were challenged with *Clostridium* spp., *E. coli*, or *Salmonella* spp. indicated that the ADFI was reduced by 16, 7, and 9%, respectively, and the ADG was reduced by 40, 10, and 29%, respectively. When the results for the challenged birds that were treated or nontreated were compared, ADFI reductions of 26.0 and 26.5% and ADG reductions of 2.9 and 21.6% were observed, respectively. Regression analyses of the ADG as a function of the protein or methionine intake of the challenged birds suggested that nutrients were diverted to the immune system. The relationship between the ΔADG and the ΔADFI was quadratic in the challenged and nontreated or treated broilers, as well as for each disease. The intercept of the regression-based curves for the data from all of the challenges were different from zero and negative (−2.20, −0.70, and −3.37, respectively), indicating that all of the challenges increased the maintenance requirements. In general, this meta-analysis allowed for the quantification of the effects of bacteriological challenges on the maintenance and feed efficiency of broiler chickens, and the knowledge that was generated in this study is applicable to broiler nutrition and for modeling their nutritional requirements.

Key words: meta-analytical study, chicken, protein, maintenance

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INTRODUCTION

Health challenges directly affect broiler production costs because they impair bird performance. *Clostridium* spp., *Escherichia coli*, and *Salmonella* spp. are the most common bacteria in commercial poultry production. Necrotic enteritis is caused by *Clostridium* ssp. and has major economic and welfare effects on poultry production (McDevitt et al., 2006). A *Clostridium* infection, particularly when subclinical, damages the bird's duodenum and jejunum, impairing nutrient digestion and absorption, and thereby negatively affecting weight gain and the feed-conversion ratio (Kaldhusdal et al., 2001; Hofacre et al., 2003; Lensing et al., 2010). Broilers that survive *Escherichia coli* challenges typically lose weight and have a poor feed-conversion ratio (Huff et al., 2006a). *Salmonella* spp., in addition to impairing performance, are a significant public health threat (Vicente et al., 2007b). This type of bacteria is one of a group that affects the function of the digestive tracts of chickens, causing diarrhea and low feed intake, as previously described. In addition, the immune system is stimulated as a secondary effect due to the intestinal damage caused by this type of bacteria.

Immune challenges affect the homeostasis of poultry due to the activation of hormones and the consequent changes in nutrient metabolism to meet the needs of

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immune functioning and tissue regeneration. Therefore, nutrients are directed to supply this increase in maintenance requirements (Latshaw, 1991). This phenomenon results in changes in the daily feed intake and daily weight gain (Shen et al., 2010; Marcq et al., 2011; Quinteiro-Filho et al., 2012). Studies of pigs have systematically quantified the effects of health challenges on feed intake and weight gain and found that these effects are determined by changes in the maintenance requirements and feed efficiency (Kipper et al., 2011; Andretta et al., 2012; Pastorelli et al., 2012). Regarding poultry, however, there are still several gaps concerning the quantification of the effects of immune challenges on their feed intake, weight gain, maintenance requirements, and feed efficiency.

Information that has been separately published in the literature does not provide a solid scientific basis for defining the feed intake and metabolic behavior of broilers because the published results are sometimes contradictory and inconclusive. We believe that meta-analysis could quantify and summarize the information in the literature. Meta-analysis fits the data to the experimental diversity, which increases the sample number, thereby showing possible differences that small populations would not be able to show. In this way, we hypothesize if it would be possible to model and to quantitatively correlate the immune response to the performance of the broilers using a Bayesian overview. Therefore, this meta-analysis was conducted to evaluate the performance responses of chickens subjected to immune challenges by different enteric bacteria (*Clostridium* spp., *Escherichia coli*, and *Salmonella* spp.) and fed diets that were supplemented or not supplemented with growth promoters, and to quantify the impact of these health challenges on maintenance requirements and feed efficiency.

MATERIALS AND METHODS

Information Systematization: Selection of Articles

The data were obtained from peer-reviewed journals. Information was extracted from the Materials and Methods and the Results sections of the preselected articles. After being identified, the papers were critically evaluated as to their quality and their relevance to the objectives of the meta-analysis. During this stage, the information contained in each selected study was analyzed, including the items related to the experimental design, treatments, studied parameters, and data analysis. The selected articles were then evaluated to determine whether to include them in the meta-analysis. The main criteria used for article selection were the following: a) experimental infection of broilers with *Clostridium* spp., *Escherichia coli*, or *Salmonella* spp., and b) performance evaluation (feed intake and weight gain). Based on these criteria, studies were independently selected by 2 evaluators. Only the data reported in articles that were published in indexed journals were selected, and their acceptance for publication was considered a subjective indication of their methodological quality. The results (negative or positive effect) were not used as selection criteria for the inclusion of studies in the database.

Database Management and Data Coding and Filtering

The data were entered in an electronic spreadsheet, with each row representing a treatment and each column representing an exploratory parameter. Information relative to the study objective (broiler performance) and other variables (genetic strain, sex, dietary nutritional composition, mortality rate, and performance parameters) were considered to allow a descriptive analysis of the studies included in the database. The database initially consisted of 91 articles, and after the exploratory analysis, 26 studies were removed because their data did not present homoscedasticity. Some of the treatments in the database involved leverage, in which case all of the data in the article should be excluded from analysis because the initial design considered all of the treatments (Lovatto et al., 2007; Sauvant et al., 2008). The criteria that were used to determine leverage followed those in the literature (St-Pierre, 2007), as shown below:

$$h_i = 1/n + (X_i - X_m)/\Sigma\ (X_i - X_m)^2,$$

where h_i is the leverage value, X_i is the value of the ith predictor variable, and X_m is the mean value of all X_i values.

The types of challenges were encoded in the database. In addition to this categorical coding, 3 other moderating codes were applied, as follows: a) a general code (study effect), with each study receiving a sequential number; b) an *inter* code, in which each treatment was encoded with the number of the general code plus another sequential number (e.g., article 1, treatment 01 = 1+01 = 101); and c) an *intra* code, which was similar to the *inter* code when there were repeated measurements (in time or doses). The dependent and independent variables were determined according to the criteria described in the literature (Lovatto et al., 2007; Sauvant et al., 2008). The challenge type was qualitatively encoded for consideration of their variability. The data were separately analyzed, and the control groups were relative to each challenge.

Description of the Database

The final database used for the meta-analysis included 65 articles that were published between 1997 and 2012 (mode: 2006), concerning a total of 86,300 broilers. The database included broilers that were challenged with *Clostridium* spp. (10,851 birds; Qureshi

et al., 1997; Hofacre et al., 1998, 2003; Bolder et al., 1999; Brennan et al., 2001, 2003; Jackson et al., 2003; McReynolds et al., 2004, 2007; Campbell et al., 2006; Chalmers et al., 2007; Gadbois et al., 2008; Kulkarni et al., 2008; Zekarias et al., 2008; Jia et al., 2009; Grilli et al., 2009; Mikkelsen et al., 2009; Liu et al., 2010), *E. coli* (4,890 birds; Edens et al., 1997; Webel et al., 1998; Li et al., 2000; Takahashi et al., 2000; Fairchild et al., 2001; Fernandez et al., 2002; Huff et al., 2002a, 2003, 2004, 2006a,b; Cheng et al., 2004; Mireles et al., 2005; Ask et al., 2006; Parmentier et al., 2006; Teo and Tan, 2006; Baurhoo et al., 2007; Arshad et al., 2008; Yang et al., 2008; Norup et al., 2009; Shen et al., 2010), and *Salmonella* spp. (45,703 birds; Cotter et al., 1998; Korver et al., 1998; Yu et al., 1999; Hegazy and Adachi, 2000; Fernandez et al., 2001; Jackson et al., 2003; Bjerrum et al., 2005; Toro et al., 2005; Hofacre et al., 2007; Ribeiro et al., 2007; Vicente et al., 2007a; Gadbois et al., 2008; Rezende et al., 2008; Zekarias et al., 2008; Al-Zenki et al., 2009; Vandeplas et al., 2009; Vilà et al., 2009; Marcq et al., 2011; Rocha et al., 2011; Faber et al., 2012; Kassem et al., 2012; Wang et al., 2012), as well as the controls (24,856 nonchallenged birds; from all of the articles). The mean values for the following parameters were calculated: initial age: 10 d (1–18 d); final age: 21 d (12–44 d), initial BW 244 g (33.6–1,800 g), final weight: 790 g (63–2,640 g), dietary ME 2,961 kcal/kg (2,900–3,604 kcal/kg), CP: 21.77% (15.2–27.33%), total lysine: 1.34% (0.88–2.04%), total methionine: 0.72% (0.39–1.62%), total tryptophan: 0.77% (0.28–1.10%), calcium: 0.97 (0.82–1.09%), and total phosphorus (0.39–0.67%). The database included 1,147 rows (treatments), of which 449 were related to the birds that received feed additives (**FA**). The groups that were treated with antibiotics were disregarded because of the difference between the actions of antibiotics in the birds.

Graphical and Correlation Analyses

A graphical analysis was used to observe the data distribution to obtain a general view of the consistency and heterogeneity of the data. Based on this analysis, correlation hypotheses were formulated to define the statistical model (Lovatto et al., 2007). During this step, the data distribution per year, country, and treatment were evaluated. The relationships between and within studies were evaluated. The average daily weight gain was regressed against the ADFI to assess the coherence of the biological data.

The outlying data points that were biologically coherent were not removed from the analyses (Sauvant et al., 2008). A correlation analysis was then conducted to determine how the results were affected by the interaction among some of the variables, and those presenting correlation were subsequently included in the ANOVA-covariance by fitting per covariate.

Variance-Covariance Analysis

Variance-covariance analyses were conducted using the GLM procedure of the Minitab 16 statistical package (Minitab Inc., State College, PA). Variance-covariance analyses were performed considering the treatments (− or + for the challenge), the general, inter-study and intra-study codes, the methionine intake, the initial age or weight, and the duration of the challenge. A residual analysis was performed graphically, and it was observed that the residues were normally distributed, with an average of zero and constant variance. Error homoscedasticity was evaluated using the tests of Hartley, Cocham, and Barlett (Ferreira, 2009), and when H_0 ($P > 0.05$), the hypothesis of residue homogeneity was assumed to be correct.

The effect of the health challenge on the feed intake and the growth rate of challenged broilers as a function of their average live weight was quantified by calculating the difference between the slopes of the equations for the control group in relation to those for the challenged group. This procedure was based on that described in the literature (Montagne et al., 2010). The difference between the 2 slopes was expressed as a percentage. The difference between the control and the challenged groups was evaluated using the *F*-test, with a CI of 95%. The broilers' response to the experimental challenge was calculated relative to the response of the control group and was expressed as a percentage of variation (**ΔADG** and **ΔADFI** are the relative variation of ADG and ADFI, respectively). This procedure was based on that described in the literature (Pastorelli et al., 2012). This method accounted for a large part of the variation within the studies. The *F*-test was used to assess the difference between the challenged and control broilers. Subsequently, the Tukey test was used to compare the mean values for all of the treatments at a 95% CI, and the probability that the average values for the performance parameters of the challenged birds were equal to the average values for the control group was rejected. Quadratic regression analysis was performed to study the response (gain) as a function of feed intake. This analysis focused on the mean effect of each challenge on the ΔADG and ΔADFI that was determined during the experimental period. This analysis considered only the effect of the challenge, as follows:

$$\Delta\text{ADG} = \alpha + (\beta_1) \times \Delta\text{ADFI}) + (\beta_2 \times \Delta\text{ADFI}^2).$$

The intercept (α) of the regression-based curves for the data reflects the reduction in the ADG that is not related to the reduction in the ADFI, which may be interpreted as an indicator of maintenance. The slope (β) reflects the extension of the change in the ADG that is associated with the reduction in the ADFI in the challenged and control broilers, indicating their feed efficiency.

RESULTS AND DISCUSSION

Effect of the Bacteriological Challenge on Broiler Performance

All of the tested challenges affected the feed intake and the growth rate relative to those of the control group (Table 1). The strongest effects were observed in broilers infected with *Clostridium* spp., which exhibited the greatest reduction in feed intake (−15.83%) and in growth rate (−40.09%) compared with those of the control group. This result is most likely due to the pathogenicity of *Clostridium*, which increases with the amount of this bacterium that is ingested (Berchieri and Macari, 2000). The analysis of the variance-covariance showed that 40% of the growth rate reduction in broilers challenged with *Clostridium* spp. is explained by feed-intake reduction. This finding is consistent with those in published studies showing that broilers suffering necrotic enteritis caused by *Clostridium perfringens* reduce their feed intake, with a consequent lower weight gain and worse feed efficiency (Kaldhusdal et al., 2001). Therefore, the observed results are coherent and indicate that feed intake reduction in the presence of *Clostridium* spp. is a protective mechanism of broilers.

When broilers were infected with *E. coli*, their feed intake was reduced by 7% and their growth rate was reduced by 10% (Table 1). These results may be related to the lesions experienced by the broilers. *Escherichia coli* causes severe liver and epithelial damage (Berchieri and Macari, 2000), thereby compromising nutrient absorption and the growth rate. The pathogenicity of the disease may be linked to the duration of the challenge because the ANOVA-covariance indicates that more than 28% of the variation is due to this variable.

Broilers infected with *Salmonella* spp. exhibited a 9% reduction in their feed intake and a 29% reduction in their growth rate. These results are consistent with previous results that reported reduced weight gain (Vandeplas et al., 2009; Marcq et al., 2011) caused by reduced feed intake and damage to the intestinal mucosa (Vandeplas et al., 2009). The ANOVA-covariance also showed that the severity of the *Salmonella* spp. infection could be largely attributed to initial age.

The studies in the literature indicated an association between age and morbidity and mortality in the broilers that were challenged with *Salmonella* spp. (Brito et al., 1995; Nakamura et al., 2002; Berndt et al., 2007), possibly due to the immature enteric immune system and the absence of normal intestinal microflora in very young broilers (Bjerrum et al., 2005; Sivula et al., 2008; Revolledo et al., 2009).

Effect of the Health Challenge on Broiler Performance: Broilers Fed FA or Not

In the analysis that considered all of the studied microbial challenges as a single challenge, a 21.6% slower growth rate and a 26.53% lower feed intake was found in the challenged broilers compared with the control group (Table 2). The broilers that were health-challenged and fed FA had a 9% slower growth rate and a 13% lower feed intake compared with the control group. The worsened performance of the challenged broilers may be attributed to their immune response requirements. Immune system activation and immune-response protein production are negatively correlated with performance (Leshchinsky and Klasing, 2001). During the acute phase of the immune response, when cytokines are released, the performance of the broilers

Table 1. Regression-based quantification of the effect of the health challenge on the rate of feed intake and the growth performance of birds challenged with *Clostridium* spp., *Escherichia coli*, and *Salmonella* spp.

	Clostridium spp.		*Escherichia coli*		*Salmonella* spp.	
Item	n[1]	Mean ± RSD[2]	n	Mean ± RSD	n	Mean ± RSD
Parameter						
Number of birds/treatment	198	775 ± 672	309	445 ± 363	213	1,576 ± 1,003
Initial age (d)	198	10.97 ± 9.437	309	9.722 ± 7.980	213	11.054 ± 10.0
Initial BW (g)	85	353.0 ± 311.8	200	248.8 ± 197.8	144	352.2 ± 230.7
Duration of the experiment (d)	148	16.622 ± 10.415	320	10.688 ± 8.027	187	14.476 ± 11.343
Response						
Feed intake reduction[3] (%)		−15.83		−7.09		−9.29
RSD		±9.10		±5.29		±2.32
Estimate *P*-value		0.01		0.01		0.04
Growth rate reduction[3] (%)		−40.09		−10.55		−29.19
RSD		±7.73		±4.57		±1.48
Estimate *P*-value		0.01		0.01		0.03

[1]Number of degrees of freedom (n).

[2]RSD = residual SD.

[3]The results are the difference between the slopes that were obtained for the challenged and nontreated (+) birds and the control birds (−; not challenged and not treated) expressed as a percentage of the slope obtained for the control birds. The difference between the control group and the challenged group was evaluated using the *F*-test, with $P \leq 0.05$, and the average age and the general code were used as fixed effects in the model. The consequences of the sanitary challenges on the daily feed intake were determined using an adjustment to the BW. *Salmonella* control: ADG = 4.768 + 95.73 × BW − 40.41 × BW^2 (R^2 = 0.99); ADFI = 23.75 + 47.78 × BW + 21.03 × BW^2 (R^2 = 0.99); *Clostridium* control: ADG = 6.180 + 67.49 × BW – 19.44 × BW^2 (R^2 = 0.80); ADFI = 8.58 + 128.9 × BW − 38.76 × BW^2 (R^2 = 0.87); *E. coli* control: ADG = −0.648 + 150.7 × BW – 92.20 × BW^2 (R^2 = 0.77); ADFI = 3.762 + 148.1 × BW – 110.6 × BW^2 (R^2 = 0.96).

Table 2. Quantification of the effect of the health challenge on the feed intake rate and the growth of challenged and treated birds and of challenged untreated birds

Response	Challenged and treated	Challenged and untreated	P-value ± RSD[1]
Feed intake Variation[2] (%)	−25.97	−26.53	0.041 ± 10.07
Growth rate Variation[2] (%)	−2.9	−21.6	0.005 ± 10.35

[1]RSD = residual SD.

[2]The results were the differences between the regression slopes obtained for the challenged and the control birds (not challenged) expressed as a percentage of the slope obtained for the control birds. The consequences of the sanitary challenges on the daily feed intake were determined using an adjustment to the BW. The difference between the control group and the challenged group was evaluated using the F-test, with $P < 0.05$, and the average age and the general code were used as fixed effects in the model. The control regression was ADG = 10.77 + 0.07173 × BWa − 0.000017 × BWa^2, $R^2 = 0.80$ and ADFI = 9.697 + 0.1042 × BWa − 0.000009 × BWa^2, $R^2 = 0.93$, where BWa is the average BW in grams.

was compromised, as shown by the reduction in their weight gain (Humphrey and Klasing, 2004). It is estimated that to meet the amino acid requirements for the synthesis of each milligram of immune response protein, 2.33 mg of muscle protein are catabolized (Reeds et al., 1994). Cheema et al. (2003) noted that broilers with a high weight-gain potential have lighter lymphoid organs. In the innate immune system, monocytes are responsible for the production of macrophages (Humphrey and Klasing, 2004), which produce signaling molecules, such as cytokines, which protect the body during the initial stage of infection. These molecules modulate local immune responses and, consequently, affect homeostasis. During health challenges, cytokines account for the reduction in feed intake and in weight gain.

In general, broilers that were challenged and fed FA presented better weight gain and feed efficiency than those that were not treated (Lensing et al., 2010; Shen et al., 2010; Amerah et al., 2012). The higher feed intake observed in the treated broilers may be attributed to the fact that some growth promoters help to fight infections by modulating the expression of cytokines in the infected birds (Faber et al., 2012). This occurrence may have positively influenced feed intake and, hence, weight gain.

Interactions Between Health and Nutrition

The CP intake did not affect the ADFI ($P > 0.05$; Table 3), whereas the ADG in the control broilers was different from that of the broilers in the treatment groups ($P < 0.05$). Figure 1 shows the equations that describe the weight gain response as a function of the CP intake (g/d). Calculating the differences among the equation slopes demonstrated that in the nonchallenged broilers, the ADG was 4.35% higher per percentage unit of CP content in diet compared with that of the challenged birds. This result may be partially attributed to the activation of the immune system in the latter group because there was a 9% increase in their nutrient utilization (Klasing, 2007).

The ANOVA-covariance revealed a quadratic response of the ADFI as a function of the methionine intake. There were no differences among the control, the challenged, and the challenged and FA-treated broilers ($P > 0.05$). The feed intake response as a function of the methionine intake exhibited a quadratic behavior [ADFI = (8.647 + 199.602) × (MI − 39.194) × MI^2, R^2 adjusted = 98.94, where MI = methionine intake]. The same procedure was used to examine the ADG values, and differences in the ADG as a function of the methionine intake were detected ($P < 0.01$), and it was found that the ADG depended on treatment for the challenges ($P < 0.01$). The ADG response as a function of the methionine intake presented a quadratic response [ADG = (10.325 + 99.317) × (MI − 27.95) × MI^2, R^2 adjusted = 93.47]. The effects of the average BW and the initial age on both variables (ADG and ADFI), but were not significant ($P > 0.05$). Normally, the amino acid requirements for the immune function are low; however, in the presence of immune challenges, nutri-

Table 3. Mean values obtained using variance-covariance analysis for the average performance of broilers that were fed additive growth promoters (FA) or not, adjusted using the covariate for methionine intake and the metabolic weight raised by the power of 0.75, using the general code as a fixed effect

Item	Control	Challenged and fed FA	Challenged and untreated	P-value ± RSD[1]
ADFI (g)	96.0[a]	96.4[a]	95.9[a]	0.005 ± 4.03
ADG (g)	55.7[a]	49.7[b]	51.6[b]	0.026 ± 3.75

[a,b]Means within a row with the same superscript do not differ according to the Tukey test ($P > 0.03$).

[1]Residual SD.

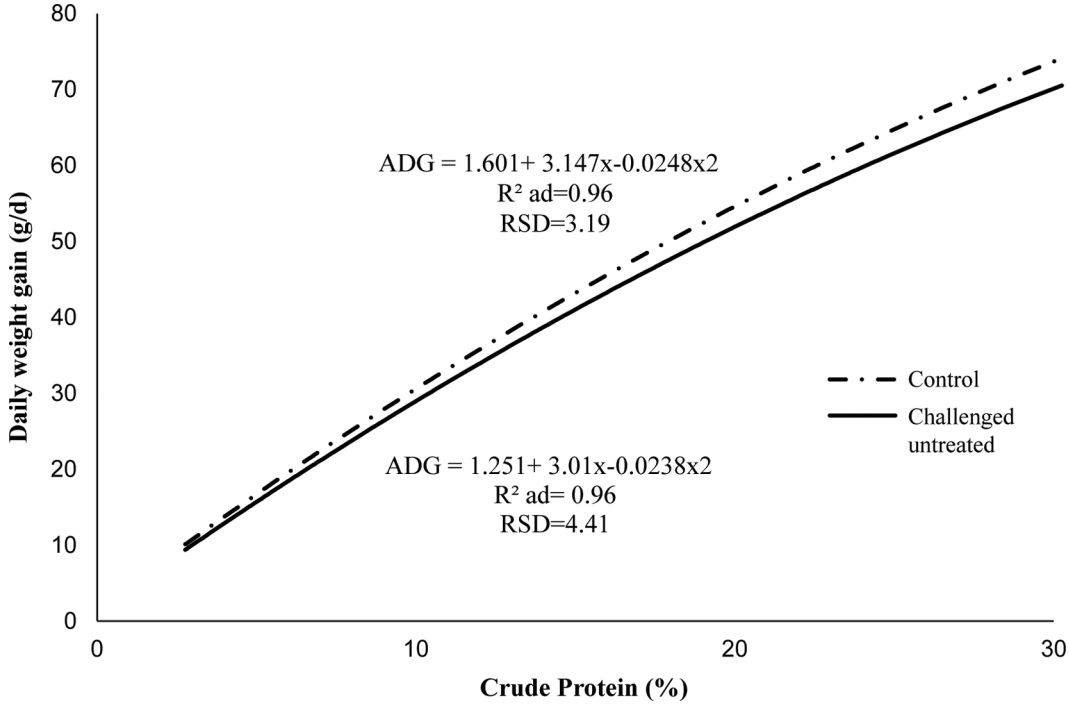

Figure 1. Equation obtained by variance-covariance analysis for average weight gain as a function of CP content in the diet adjusted by covariate for age. RSD = residual SD; R^2ad = R^2 adjusted.

ents, particularly amino acids, are diverted to nourish the innate immune system, increasing the bird's requirements (Klasing, 2007). The acute phase of the immune response requires more amino acids and more energy than those used by leukocytes, and the synthesis of proteins such as haptoglobin, α-macroglobulin, and ceruplasmin is prioritized relative to muscle protein synthesis (growth).

The first study relating the dietary methionine level with the immune response in broilers was conducted by Bhargava et al. (1971). These authors reported that 0.4% dietary methionine promoted the immune response and that 0.7 and 1.1% levels improved the weight gain and the feed conversion ratio. An 80% increase in the methionine levels in the diet of broilers that were challenged with *E. coli* improved their weight gain, but did not change their feed intake (Klasing and Barnes, 1988). More recent studies (Swain and Johri, 2000; Shini et al., 2005) indicated that the methionine requirements to enhance both the immune response and the performance are higher than those needed to improve only the performance. It is possible that the lower weight gain per gram of methionine intake in the challenged broilers results from changes in the partitioning of this amino acid because the priority is to supply the protein synthesis requirements for the immune response and not for protein deposition in muscles. The immune-response enhancing effect of higher dietary methionine levels may be explained by the sensitivity of the cell-proliferation process to glutathione and cysteine, which are methionine metabolites (Shini et al., 2005).

Relationship Between the Growth Rate Reduction and Feed Intake

The relation between the ΔADG and the ΔADFI was quadratic for the challenged FA-fed broilers and the challenged nontreated broilers (Figure 2), as well as for each disease (Figure 3). In the regression equation-based curve for the challenged and nontreated broilers, the intercept was different from zero and negative. This finding means that at the same ΔADFI point, the ΔADG is lower (−3.5%), demonstrating an increase in their maintenance needs. The slope of the curvilinear response indicated that the feed efficiency worsened as the ΔADFI increases. Birds that were challenged and fed FA did not increase their maintenance requirements (0.74); however, the curvilinear response showed that feed intake reduction worsened feed efficiency. The intercepts of the data for each of the challenges (*Salmonella* spp., *Clostridium* spp., and *E. coli*) were different from zero and negative (−2.20, −0.70, and −3.37, respectively), indicating that all of the challenges increased the maintenance requirements. Moreover, the curvilinear response showed that the higher the reduction in ΔADFI, the worse the feed efficiency for all of the health challenges.

A reduced growth rate is commonly attributed to a reduced ADFI, but in the case of the health challenges, growth may be impaired due to an increase in the requirements for the metabolic and digestive processes (Sandberg et al., 2007). Moreover, part of the reduction in the ADG may be attributed to an increase in the

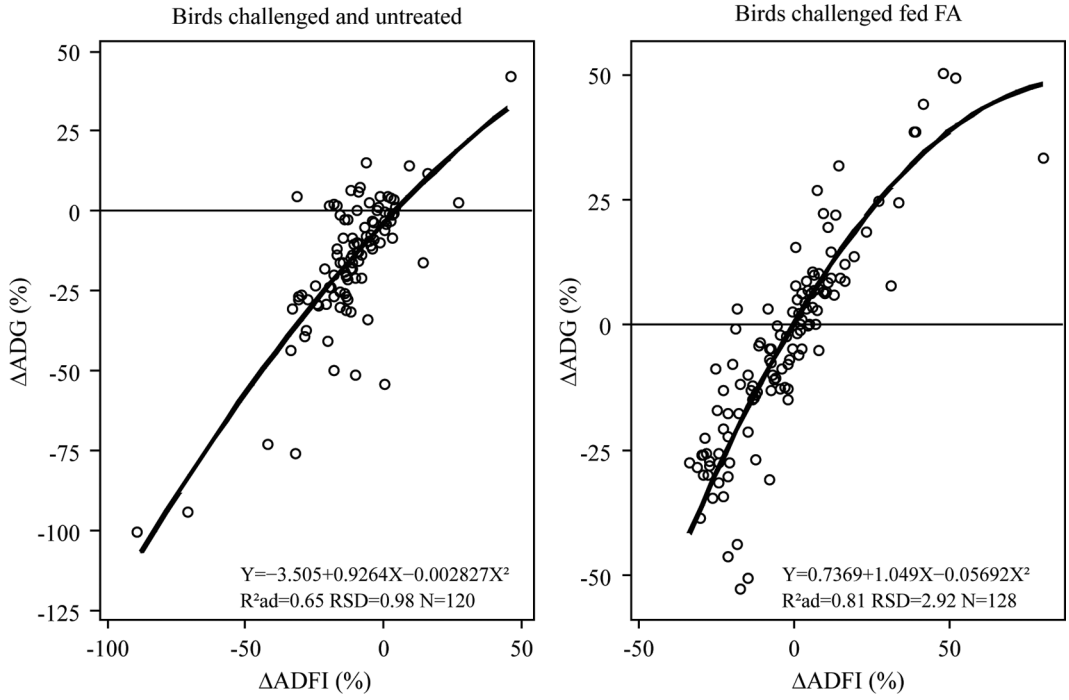

Figure 2. Relationship between the change in the growth (ΔADG) and feed intake (ΔADFI) in chickens challenged with intestinal bacterial infections in birds untreated and fed additive growth promoters (FA) obtained by regression. N = number of treatments, RSD = residual SD; R^2ad = R^2 adjusted.

metabolic requirements associated with stimulation of the immune system (Sandberg et al., 2007). The feed intake of broilers that are subjected to health challenges typically decreases, but the cause of this phenomenon and its intensity vary according to the pathogenicity of the infectious agent (Pastorelli et al., 2012). In most

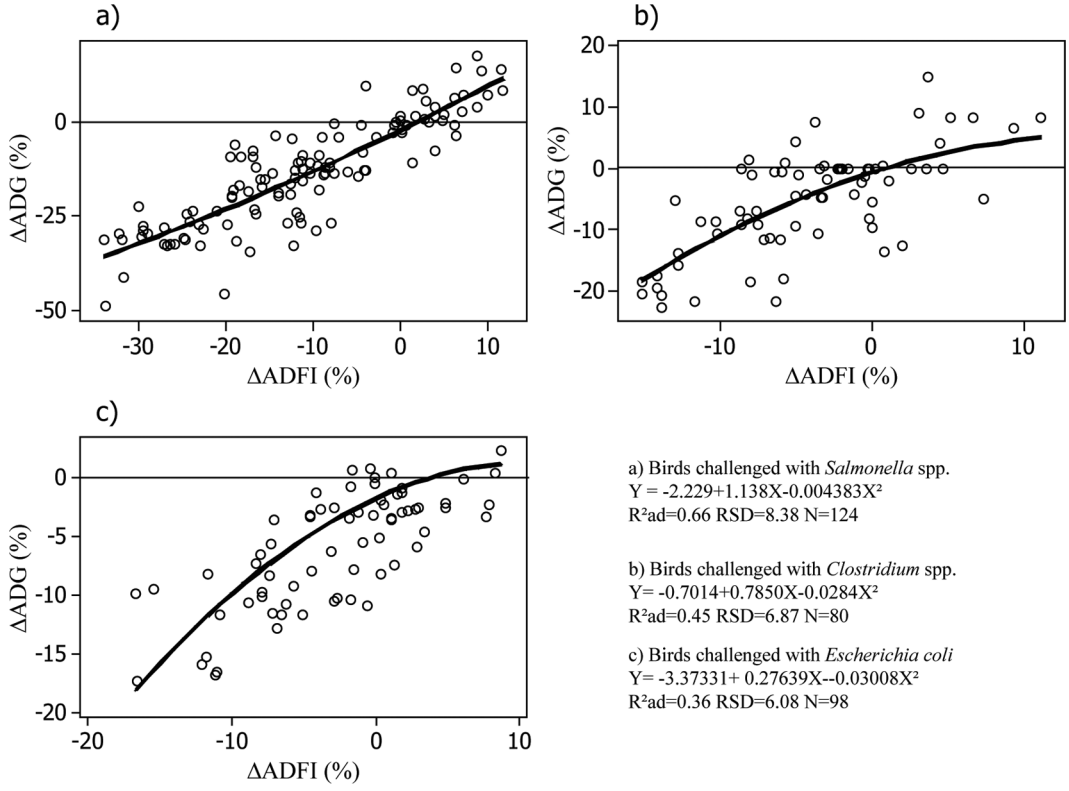

Figure 3. Relationship between the change in the growth (ΔADG) and feed intake (ΔADFI) in chickens challenged *Salmonella* spp. (a), *Clostridium* spp. (b), and *Escherichia coli* (c) obtained by regression. N = number of treatments, RSD = residual SD; R^2ad = R^2 adjusted.

instances, the reduced feed intake results from the activation of the innate immune response during the acute phase, which is mediated by cytokines (Klasing, 1998). The lower ADFI and the increase in the nutritional requirements associated with the activation of the immune system alter the nutrient flow and cause changes in the metabolism of several organs (Klasing, 1998).

The metabolic changes caused by health challenges and the responses that involve alterations in nutrient partitioning due to changes in the maintenance requirements and in nutrient utilization efficiency need to be further investigated in quantitative terms. In general, this meta-analysis allowed for the quantification of the effects of bacteriological challenges on broiler maintenance and feed efficiency, and the generated knowledge from this study is applicable to broiler nutrition and for modeling their nutritional requirements.

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