ized ileal digestible (SID) AA supply. The minimum of energy and AA allowable milk estimates and their mean were calculated. A first-limiting nutrient model (minimum of energy and AA allowable milk) had an RMSE of 110%. A co-limiting nutrient model (mean of energy and AA allowable milk) had a lower (32%) RMSE. To more fully investigate the utility of a co-limiting nutrient model, a multisubstrate Michaelis–Menten equation was fit to predict milk yield as a function of AA and ME supply. After a stepwise elimination of nonsignificant parameters, the final model (based on Arg, Leu, Met, Phe, Thr, and Val SID intake) returned a RMSE of 10% and very good concordance (0.77). These results suggest that nutrients co-limit milk production and that moving toward a more response-driven model may help define more precise diets that account for dynamic mammary uptake of AA.

Key Words: amino acid, lactating sow, variable efficiency

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041 Citrulline and de novo arginine synthesis in perinatal and young pigs. J. C. Marini[1,2,*], U. Agarwal[1], I. C. Didelija[1], B. Stoll[1], D. G. Burrin[1], *[1]USDA-ARS Children's Nutrition Research Center, Baylor College of Medicine, Houston, TX, [2]Section of Critical Care Medicine, Baylor College of Medicine, Houston, TX.*

Arginine is a conditional essential AA that becomes essential when its demand (e.g., growth, disease) exceeds its production. The endogenous synthesis of arginine is a multiorgan process where citrulline synthesized by the gut is utilized by 2 renal enzymes (argininosuccinate lyase [ASL] and argininosuccinate synthase [ASS]) to produce arginine. Because ASS and ASL are present in the gut of neonatal pigs, it is believed that the intestinal–renal axis for arginine synthesis is not functional in the newborn. However, this is not consistent with the high plasma citrulline concentrations seen in perinatal pigs. To address this apparent paradox, we measured citrulline production and concentrations in premature (P-10; 10 d preterm and 1.0 ± 0.1 kg BW), neonatal (P8; 8 d and 2.5 ± 0.2 kg BW), and young pigs (P30; 30 d and 7.5 ± 0.3 kg BW). We also used stable isotopes to study the interorgan production of citrulline and arginine in neonatal and young pigs. Premature pigs (P-10) have a reduced ($P < 0.001$) ability to produce citrulline (23 ± 2 μmol·kg^{-1}·h^{-1}) when compared with older animals (74 ± 4 and 41 ± 3 μmol·kg^{-1}·h^{-1} for P8 and P30, respectively). Plasma citrulline concentrations, however, were not different ($P = 0.31$; 171, 190, and 145 μmol/L for P-10, P8, and P30, respectively). A substantial dilution of the citrulline tracer in the portal circulation of P8 and P30 pigs indicated enteral citrulline production. Likewise, the appearance of labeled arginine in the renal vein demonstrated citrulline utilization for arginine synthesis by both age groups. Based on the labeling pattern of the arginine released by the PDV, we were unable to detect any arginine synthesis by the gut; the arginine released by the PDV was likely to originate from protein breakdown because the essential AA phenylalanine was also released. The quantitation of organ fluxes indicated a production of 22 ± 7 and 21 ± 7 μmol of citrulline/L blood flow by the PDV (P8 and P30, respectively) and a renal conversion into arginine of 19 ± 7 and 16 ± 5 μmol/L blood flow, respectively. This demonstrates that the intestinal–renal axis for arginine synthesis is present in the neonatal pig. Although ASS and ASL were present in the small intestine of P8 pigs, they were localized in the tip of the villus whereas the enzymes responsible for the synthesis of citrulline were present in the base and crypt. The lack of co-localization of these enzymes prevents the gut from synthesizing arginine and explains the high levels of circulating citrulline observed in perinatal pigs.

Key Words: arginine, citrulline, neonate, pig, tracer

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042 An update on modeling dose–response relationships: Accounting for correlated data structures and heterogeneous variance in linear and nonlinear mixed models. M. A. D. Goncalves, N. M. Bello*, S. S. Dritz, M. D. Tokach, J. M. DeRouchey, J. C. Woodworth, R. D. Goodband, *Kansas State University, Manhattan*.

Advanced methods for dose–response assessments are used to estimate concentrations of a nutrient that optimize a given outcome of interest, thereby determining nutritional requirements for optimal performance. Traditionally, many dose–response methods use a fixed-effects framework that assumes mutually independent observations with homogeneous variances. Yet experimental data often present a design structure that includes correlations between observations (e.g., blocking, nesting, etc.) as well as heterogeneity of variances that can mislead inference if disregarded. Our objective is to demonstrate practical implementation of computationally intensive linear and nonlinear mixed models methodology to describe dose–response relationships accounting for correlated data structure and heterogeneous variances. To illustrate, we model data from a randomized complete block design study to evaluate the standardized ileal digestible (SID) Trp:Lys dose–response on G:F of nursery pigs. A base linear mixed model was fit to explore the functional form of G:F relative to Trp:Lys and assess model assumptions, in particular residual homoscedasticity. Next, we fitted 3 competing dose–response mixed models to G:F, namely a quadratic polynomial (QP), a broken-line linear (BLL) ascending model, and a broken-line quadratic (BLQ) ascending model, all of which included heteroskedastic specifications, as dictated by the base model, and used parameter estimates from the base model as initial values. The GLIMMIX procedure of SAS (version 9.4; SAS Inst. Inc., Cary, NC) was used to fit the base and QP models and the NLMIXED procedure was used to fit the nonlinear models. We further illustrate the use of a grid-search approach to facilitate convergence and parameter estimation in nonlinear mixed

models, as this seemed to be the most common implementation problem. Model fit between competing dose–response models was compared using maximum likelihood–based Bayesian information criterion (BIC). The QP, BLL, and BLQ models fitted on G:F of nursery pigs yielded BIC values of 353.7, 343.4, and 345.2, respectively, indicating a better fit of BLL followed closely by BLQ. The BLL breakpoint estimate of the SID Trp:Lys was 16.5% (95% confidence interval [CI] 16.1–17.0), whereas the BLQ estimate was 16.0% (95% CI 15.5–16.6). Importantly, accounting for heterogeneous variance enhanced inferential precision as the breadth of the CI for mean breakpoint decreased by approximately 44%, from 95% CI 15.8 to 17.4 to 95% CI 16.1 to 17.0 SID Trp:Lys. In summary, we illustrate the use of linear and nonlinear mixed models for dose–response relationships accounting for heterogeneous residual variances, discuss important diagnostics and their implications for inference, and provide practical recommendations for computational troubleshooting.

Key Words: dose–response, heterogeneous variance, linear and nonlinear mixed models

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043 Effects of standardized ileal digestible valine-to-lysine ratio on growth performance of twenty-five– to forty-five–kilogram pigs under commercial conditions. M. A. D. Goncalves[1,*], M. D. Tokach[1], S. S. Dritz[1], N. M. Bello[1], K. J. Touchette[2], R. D. Goodband[1], J. M. DeRouchey[1], J. C. Woodworth[1], *[1]Kansas State University, Manhattan, [2]Ajinomoto Heartland, Inc., Chicago, IL*.

Two experiments were conducted to estimate the standardized ileal digestible (SID) Val:Lys requirement for growth performance in 25- to 45-kg pigs. In Exp. 1, 1134 gilts (PIC 337), initially 31.2 kg (SD 2.0) BW, were used in a 19-d trial with 27 pigs/pen and 7 pens/treatment. In Exp. 2, 2100 gilts (PIC 327), initially 25.4 ± 1.9 kg BW, were used in a 22-d trial with 25 pigs/pen and 12 pens/treatment. In both experiments, treatments were blocked by initial BW in a randomized complete block design. In Exp. 1, there were 6 treatments with SID Val:Lys at 59.0, 62.5, 65.9, 69.6, 73.0, and 75.5%. For Exp. 2, there were 7 treatments with SID Val:Lys at 57.0, 60.6, 63.9, 67.5, 71.1, 74.4, and 78.0%. Diets were formulated to ensure that Lys was the second limiting AA throughout the experiments. Responses were analyzed separately for each experiment using general linear and nonlinear heteroskedastic mixed models, including initial BW as an explanatory covariate and BW block as a random effect. In Exp. 1, ADG linearly increased with increasing SID Val:Lys ($P = 0.009$; 680, 717, 717, 712, 744, and 726 ± 17.1 g, respectively), whereas no significant treatment differences were observed for G:F (0.467, 0.467, 0.472, 0.474, 0.481, and 0.472 ± 0.0084, respectively). In Exp. 2, ADG (quadratic, $P = 0.002$; 621, 662, 717, 708, 708, 726, and 717 ± 16.1 g, respectively) and G:F increased (linear, $P < 0.001$; 0.415, 0.420, 0.437, 0.429, 0.433, 0.441, and 0.439 ± 0.0046, respectively) with increasing SID Val:Lys. There was no evidence of experiment × treatment interaction. Therefore, data from the 2 experiments were combined for analysis using experiment and BW block within experiment as random effects. Competing models, namely a broken-line linear model, a broken-line quadratic model, and a quadratic polynomial (QP), were compared using Bayesian information criterion. In the combined analysis, the best-fitting model for ADG was a QP (prediction equation: $-1.15 + 4.13 \times$ SID Val:Lys $- 2.78 \times$ SID Val:Lys$^2 + 0.012 \times$ initial BW) with optimum ADG estimated at 74.4% (95% confidence interval [CI] 69.5 to > 78.0) SID Val:Lys. The best-fitting model for G:F was also a QP (prediction equation: $-0.04 + 1.36 \times$ SID Val:Lys $- 0.94 \times$ SID Val:Lys^2) with optimum G:F estimated at 72.3% (95% CI 64.0 to > 78.0) SID Val:Lys. In conclusion, 67% SID Val:Lys was able to capture 99% of maximum ADG and G:F in 25- to 45-kg pigs.

Key Words: growth, pig, valine

Table 043. Standardized ileal digestible Val:Lys ratio at different performance levels

	Percent of maximum performance			
Item	95%	97%	99%	100%
ADG	58.9	62.3	67.3	74.4
G:F	< 57.0	60.4	65.5	72.3

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044 Determination of lysine adequacy on a population basis for growing pigs. C. E. Zier-Rush[1], C. Neill[2], S. B. Jungst[2], N. Matthews[2], D. S. Rosero[1,*], R. D. Boyd[1], *[1]The Hanor Company, Inc., Franklin, KY, [2]PIC, Hendersonville, TN*.

Nutrient requirements are primarily determined for a growth phase and mean population without considering population variation and important variables that define population response. For lysine curves to be financially useful, responses must be established using multiple criteria and equations must be developed for financial modeling. This study defined the response to 4 standardized ileal digestible (SID) lysine curves using 6 population growth (whole-body and carcass) and carcass primal parameters. A total of 2048 pigs (PIC Camborough × TR-4 or 327) were used in a growth assay from 20.4 (± 0.3 kg) to 119.0 (± 1.1 kg) with a fixed-time end point (110 d). Pigs were placed in 65 pens (30 to 32 pigs/pen and 0.70 m^2/pig), blocked by BW, and randomly allotted within gender and genotype to 4 dietary treatments administered in 5 phases of growth (20 kg BW phases). Dietary treatments corresponded to 4 different SID lysine curves that deviated from the 2008 PIC lysine specifications. Curves were 92, 98, 104, and 110% of the PIC standard lysine curve {SID lysine:ME [g SID lysine/Mcal ME (NRC, 1998)] = $(2.7 \times 10^{-5} \times \text{BW}^2) - (0.0153 \times \text{BW}) + 4.114)$}. Diets were corn–soybean meal based with 15.0% corn distiller's dried grains with solubles and 2.7% choice white grease as a fat source. Major ingredi-