Is lysine:methionine always important?

While the estimated factorial requirements for lysine to methionine may be approximately a 3:1 ratio, there is ample proof that each amino acid has to be supplied individually to meet the needs of the animal.

By **ESSI EVANS** and **ROBERT J. PATTERSON***

IDEAL amino acid ratios have been used to formulate diets for swine and poultry since Wang and Fuller (1989) introduced the concept for growing pigs.

One amino acid, generally lysine, is set as the standard, and the assumed need for other amino acids is expressed as percentages or ratios of the standard amino acid. Then, after the rate of protein deposition is assessed, lysine content is predicted. After correcting for metabolic losses and digestibility, the actual feeding amounts can be determined for formulation from the ratios.

There are several recognized advantages to this system. For growing pigs, lysine is generally the first limiting amino acid in cereal-soybean meal diets. By formulating for lysine rather than protein, the other essential amino acids are in excess, and the animals' needs are met.

A slight excess in amino acids has not been shown to be detrimental to the performance of pigs or poultry. For example, if the value for methionine is set at 30% of lysine, then 35% will not be detrimental, provided lysine meets the projected need. Furthermore, the system permits the user to predict the rate of protein deposition when lysine or another amino acid is available at below the suggested level.

Later research revealed that different ratios are required for young, immature animals versus larger, finishing animals as well as growing males versus growing females (Baker, 1996). This variation is associated with the difference in amino acid profile required for maintenance as opposed to lean tissue growth.

For poultry, the rate of feather growth is further consequential. The amino acid profiles needed for maintenance and for feathering have been shown to be different from the profile needed to produce optimum weight gains (Hruby et al., 1994).

Other inconsistencies inherent to such an oversimplified system have been documented. Changes in the amino acid patterns have been shown to occur due to environmental factors (Brake et al., 1998; Ferguson and Gous, 2002), undersupply of non-essential amino acids (Kerr and Kidd, 1999) as well as any factors influencing protein turnover rate (Whittemore et al., 2001).

Factorial requirements for amino acids for both maintenance and growth are now increasingly being used in order to take into account issues that cannot be addressed by ideal amino acid ratios. Included are intake, growth rate and environment (Oviedo-Rondon and Waldroup, 2002) as well as other factors that alter the relationship of amino acids to each other.

Ratio in ruminants

Rulquin and coworkers at INRA in France (1993) outlined a system to provide an ideal ratio of lysine and methionine as a proportion of the protein truly digested in the intestine (PDI). The requirements of these amino acids were thus calculated on a relative rather than an absolute amount.

Through their analyses of 164 feed treatments, Rulquin et al. showed that milk protein yield responds to both methionine and lysine. Production of milk or protein increased in response to the addition of either amino acid and then reached a plateau. This indicates that an excess of either amino acid would result in a reduced efficiency of use but would not reduce milk protein output, i.e., would not have a detrimental effect on production.

Rulquin et al. are often credited as being the origin of a ratio between lysine and methionine, and this may be a misinterpretation. The ratio was established with respect to PDI and was not a ratio of lysine to methionine. Furthermore, the research has been interpreted to mean that performances will be optimized when lysine and methionine constitute a specific ratio of PDI, regardless of PDI relative to requirements and regardless of the metabolic status of the animal. Again, these researchers made careful note of the fact that, in almost all cases, protein needs of the cow and the rumen were met in their many studies.

In addition, Rulquin et al. analyzed a large number of points (164) for each variable. However, the data showed that there was a very narrow coefficient of variation (CV). The low CV (Table 1) suggests that, even though the data covered a wide range, most of the points were about the mean. All trials involved Holstein cows, and 81% of the trials were conducted in early lactation. Requirements for absorbable protein were largely met in all of the studies.

Some of the misconceptions surrounding the origins of the requirement for a specific amino acid ratio may have resulted in overemphasizing the importance of this ratio. The PDI system shows that the efficiency of use of amino acids can be reduced when they are available at levels above requirements, but it was not suggested that this would be detrimental to performance. Deviations in amino acid ratios may be unavoidable using least-cost ration formulation systems in order to generate an economically feasible result.

Uses for other functions

Many models and ration-balancing programs calculate the requirements of amino acids based solely on their use for maintenance and for new protein synthesis (milk, muscle and fetus). Amino acids contribute to the well-being of animals through many other biological reactions, and these reactions influence the supply available for maintenance and protein synthesis. These uses of amino acids undoubtedly change the post-absorptive ratio between amino acids being supplied to animals as their circumstances change.

Methionine and cystine. It is an accepted practice by nutritionists in formulating feeds for non-ruminants to establish specifications for methionine and for methionine plus cystine. This acknowledges the ability of methionine to supply

*Dr. Essi Evans is with Essi Evans Technical Advisory Services Inc. Dr. Robert J. Patterson is with Papillon Agricultural Co. The full article plus additional tables appear at www.feedstuffs.com.

cysteine, if it is limiting. Cysteine molecules combine, resulting in dicysteine or cystine. Both methionine and cystine are classified as essential but are closely linked to the status of each other. Methionine can be used in place of cystine, but the reverse reaction does not occur.

By only considering requirements for methionine and not methionine plus cystine, there is an information void concerning the effects that synthesis of cystine might impose on the available methionine pool. Both sulfur-containing amino acids should be considered together. A ratio of methionine, but not methionine plus cystine, to any other relative nutrient would not be fully meaningful.

Methionine in methyl donor reactions. Kelly (1996) showed that the need for methionine changes with the availability of other methyl donor compounds. The compound required in greatest quantities is choline.

Emmanuel and Kennelly (1984) and Lobley et al. (1996) demonstrated that up to one-third of the total methionine supply could be lost due to the need to synthesize choline.

Methionine as a lipotropic agent. Methionine is also a lipotropic agent, increasing the rate of phospholipid synthesis. The use of methionine to assist in the mobilization of lipids may change with the availability of other lipotropic agents, such as choline, and by the amount of lipid being transported.

The lipotropic effect of methionine may be one explanation for increases in milk fat percentages when methionine is supplied above assumed requirements. As a result, strictly calculating the need for methionine, based upon its usage to support tissue protein and milk production, may underestimate needs. Also, such uses would tend to vary, thereby changing methionine relative to lysine and the ability of both to support lactation.

Oversupply

While levels of lysine above requirements are relatively innocuous, methionine has been shown to be toxic (Benevenga, 1974) when provided to animals at levels substantially above requirements, resulting in reduced feed intake and reduced production (Abe et al., 2000).

The toxic effect has been associated with hepatic accumulation of S-adenosylmethionine. This may be partially alleviated if excess levels of branched-chain amino acids are also available to contribute to transulfuration reactions (Abe et al., 1999), but there appears to be no relationship with lysine.

Calves appear to be able to tolerate about twice their methionine requirements for maximum weight gains (Abe et al., 2000). However, feed intakes in dairy cows declined when abomasally infused methionine was above about 0.65% of dry matter intake and hydroxy methyl butanoic acid (HMB; methionine hydroxy analog) intakes exceeded 1% of dry matter intake. Levels quoted do not include amounts in the basal diet.

Experimental results. Feeding trials have been conducted with either methionine or lysine supplied at levels above calculated requirements, resulting in altered ratios between lysine and methionine. Sklan and Tinsley (1996) added rumen-protected HMB to diets of lactating cows (Table 2). The ratio of lysine to methionine fell from 3.1:1 to 2.7:1. There were no detrimental effects noted.

Guinard and Rulquin (1995) provided up to 32 g of abomasally infused methionine to lactating cows (Table 3). In this experiment, lysine was held constant, while methionine was varied. The differences in milk protein between treatment 1 and the remaining treatments reveal that the cows are sensitive to methionine. However, oversupplying methionine (treatment 4) had no adverse effects.

Varvikko et al. (1999) infused 10, 20, 30 and 40 g of methionine above assumed requirements to lactating cows without affecting intake or performance. In the same study, lysine was oversupplied by 15, 30, 45 and 60 g. Again, shifts in the ratio between lysine and methionine did not influence production or intake.

While there were no productive advantages of oversupplying either lysine or methionine alone, the need to maintain a constant ratio suggests that a benefit would result when these two amino acids are increased in tandem. Robinson et al. (1998) fed cows a control diet, one that oversupplied lysine and one where methionine was oversupplied along with lysine. Maintaining a specific ratio did not influence performance (Table 4).

A subsequent study by Robinson et al. (2000) showed a decline in intake and milk production when metabolizable methionine was increased by a calculated 40% over requirements.

1. Intake and production of cows in 57 trials and 164 diets

Item	Mean	CV, %	Range
Dry matter intake, kg per day	19.4	10.5	14.6-25.1
Crude protein, % of dry matter	15.2	11.2	10.7-19.1
Lysine, % of PDI	6.9	13.0	5.0-10.6
Methionine, % of PDI	2.2	13.6	1.7-2.7
Bodyweight	593	5.3	510-675
4% fat-corrected milk	28.1	13.8	19.3-35.2
Milk protein, %	3.02	5.2	2.63-4.62
Milk fat, %	3.66	13.3	2.63-4.62

2. Addition of HMB on intake and milk production

	Treatment	
Item	Control	HMB
Dry matter intake, kg	22.2	21.8
Milk, kg	42.5	43.8
Fat, %	2.82	2.83
Protein, %	2.77	2.78
Methionine supply, g	55.8	64.4
Lysine supply, g	173	172
Methionine requirement, g	54.5	54.5
Lysine requirement, g	163.5	163.5

3. Addition of methionine on intake and milk production

	Treatment			
Item	1	2	3	4
Methionine infused, g	0	8	16	32
Dry matter intake, kg	17.0	17.1	17.1	17.0
Milk, kg	24.2	23.2	24.3	24.0
Fat, %	4.06	4.17	4.12	4.26
Protein, %	2.77	2.87	2.91	2.88
Methionine requirement, %	70	80	100	140

4. Addition of lysine or lysine+methionine on intake and production

	Treatment		
Item	Control	+21 g lysine	+22 g lysine, +6 g methionine
Dry matter intake, kg	23.3	23.0	23.3
Milk, kg	33.9	33.5	33.9
Fat, %	3.79	3.80	3.85
Protein, %	3.21	3.21	3.26
Bodyweight change	0.35	0.38	0.30
Lysine requirement, %	100	113	113
Methionine requirement, %	114	113	141

Abomasally infusing additional lysine to the diet did not statistically change performance relative to the control, whereas adding high levels of methionine reduced intake and milk yield. The last treatment clearly shows that providing increased levels of lysine to maintain a lysine:methionine ratio did not alleviate the adverse effect of high dietary methionine.

Conclusion

While the estimated factorial requirements for lysine to methionine may be approximately a 3:1 ratio, there is ample proof that each amino acid has to be supplied individually to meet the needs of the animal. Lysine and methionine are key amino acids needed for production and a host of other biochemical functions. Feeding lipids may spare lysine.

Methionine can be used to form cystine, it can be used as a methyl donor in place of choline and it is a lipotropic agent, again interacting with choline. All of these reactions alter the amount available for protein synthesis. The mammary gland is also capable of changing blood flow rates and extraction rates of the amino acids in response to high or low blood amino acid levels.

The addition of these nutrients that have sparing effects has an impact on the overall levels of lysine and methionine that the cow needs. This makes it difficult to precisely know the requirements. However, practical formulation systems need to meet the amino acid requirements without elevating costs. An excess of one or the other of these two amino acids, within formulation limits, is acceptable if it is the lowest-cost solution because it will not affect production.

References

For the full article and complete list of references, visit www.feedstuffs.com or e-mail tlundeen@feedstuffs.com.