Asian-Aust. J. Anim. Sci.
Vol. 19, No. 9 : 1361 - 1368
September 2006

www.ajas.info

Amino Acid Imbalance-Biochemical Mechanism and Nutritional Aspects

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ABSTRACT : Amino acid imbalances refer to the deleterious effects that occur when a second-limiting amino acid or mixture of amino acid lacking a particular limiting amino acid is supplemented in diets marginal in one or more indispensable amino acids. In spite of variation in the conditions that have been used to induce amino acid imbalances, such as protein level in the diet, the extent of difference in total nitrogen content between basal and imbalanced diets, and kinds of amino acids used as imbalancing agents, the conspicuous common features of amino acid imbalances have been a decreased concentration of the limiting amino acid in blood, depression of feed intake and weight gain, and increased dietary content of the limiting amino acid needed to correct the imbalances. There is strong evidence that a decrease in the concentration of a limiting amino acid detected in the anterior prepyriform cortex of the brain is followed by behavioral effects, especially a decrease in feed intake. This might be due to the competition between the limiting amino acid and the amino acids in the imbalancing mixture for transport from blood into brain. One of the biochemical responses of animals fed amino acid imbalanced diets is a rapid decrease in the concentration of the limiting amino acid, which are due in part to an increase in catabolism of the limiting amino acid by the increased activities of enzymes involved in the catabolism of the amino acid. Practically, specific amino acid imbalances could be induced in swine and poultry diets that have been supplemented with lysine, methionine, tryptophan when threonine, isoleucine, valine, etc. are potentially third- or fourth-limiting in diets. In these cases supplementation of the limiting amino acid could be beneficial in preventing the decrease of feed intake that could otherwise occur as a result of amino acid imbalance. (**Key Words :** Amino Acid Imbalance, Feed Intake, Growth Rate, Enzymes)

INTRODUCTION

The concept of amino acid balance had been introduced by two pioneering researchers, Osborne and Mendel (1914). They understood that the nutritional value of a protein was dependent upon the proportions of the various indispensable amino acids it contained. Harper (1964) categorized the adverse interaction of disproportionate balance of amino acids as imbalances, antagonisms, and toxicities.

According to Harper's definitions, imbalances refer to the deleterious effects that occur when a second-limiting amino acids or a mixture of amino acids lacking the limiting amino acid is supplemented to diets marginal in one or more indispensable amino acids. The adverse effects of the imbalanced diet may be alleviated by the addition of the most limiting amino acid to the diet.

The current view of amino acid imbalance holds that the decrease of a limiting amino acid in plasma or altered ratio of limiting amino acid to total amino acids is detected in the anterior prepyriform cortex of brain. This is due in part to the competition between the imbalanced amino acids and the imbalancing amino acids for transport from blood into brain. A decrease in the concentration of a limiting amino acid in specific regions of the brain is followed by behavioral effects, especially a decrease in feed intake (Gietzen, 1993). There have been unanswered questions, however, as to the metabolic fate of a limiting amino acid, for example, what causes the blood level of limiting amino acid to decrease?

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Received April 18, 2006; Accepted June 19, 2006

AMINO ACID INTERACTION

Harper reported his categories of amino acid interactions in 1956. He restricted the term "amino acid imbalance" to cases in which a detrimental effect is observed when a diet low in one or more of the indispensable amino acids was supplemented with other amino acids or protein, and the effects were prevented by a small supplement of the amino acid that is the most limiting. Antagonisms were defined as those interactions in which the ingestion of excessive amounts of one amino acid increases the requirement for a structurally related amino

acid. As in the case of imbalances, the structurally related amino acid must be provided to alleviate the effect of the antagonism. Toxicities were defined as a conditions caused by feeding excessive quantities of individual amino acids that are not prevented by supplementing diets with other amino acids or groups of amino acids.

AMINO ACID IMBALANCE DEVELOPMENT OF THE CONCEPT

The term "amino acid imbalance" was first used by Hier, et al. (1944). They observed growth depression of rats fed a diet containing excessive concentrations of individual amino acids such as glycine, phenylalanine, and proline and attributed the effects to amino acid imbalances. Subsequently, a number of investigators reported that the growth rate of animals fed a low-protein, tryptophan deficient diet was depressed by supplementation of protein sources like corn and gelatin deficient in tryptophan. They also suggested that an amino acid imbalance induced by excessive amounts of other amino acids in the diet increased the requirement for the most limiting amino acid.

It was believed that only indispensable amino acids, not dispensable amino acids might induce imbalance. However, amino acid supplements of dispensable amino acids such as alanine, glycine, serine, proline, glutamate, and aspartate decreased weight gains. Much larger amounts of dispensable amino acids were required to depress growth than needed with indispensable amino acids (Savage and Harper, 1964; Tews et al., 1979, 1980).

Most of the earlier investigators applied the concept of amino acid imbalance in their research using a variety of low protein diets. With the low protein diets used, imbalances could be produced by adding to the low protein diet a second-limiting amino acid or mixture of individual amino acids lacking the most limiting indispensable amino acid. Generally, the adding method of amino acid mixture tended to consistently induce strong imbalance and maximize associated metabolic changes.

However, supplementation of individual or groups of indispensable amino acids in control diets containing adequate dietary protein appeared to show typical consequences of amino acid imbalances (Calderon and Jensen, 1990; Davis and Austic, 1994; Park and Austic, 1998, 2000). Because responses can occur in conventional poultry at adequate dietary levels of protein, it is likely that amino acid imbalance is a phenomenon that can be important for the practical consideration in animal nutrition.

APPLYING THE CONCEPT TO A SPECIFIC AMINO ACID

Even though the supplementation of diets with excessive amounts of amino acids to induce imbalances is not a normal conditions, such approaches may provide some information as to which amino acids are suspect under practical conditions. It is more difficult to determine the nature of much subtler imbalances that might occur under conditions of practical nutrition.

After the phenomenon of amino acid imbalance was accepted as a general condition in protein metabolism, researchers focused on imbalances of other indispensable amino acids such as threonine, histidine, lysine, isoleucine, and methionine. There has been much interest in the dietary imbalance of threonine in the fact that threonine might be limiting in the diets of several species including humans, rats, pigs, and poultry. These have become useful models for investigations into the physiological and metabolic mechanisms of amino acid imbalance.

Isolucine is the fourth-limiting amino acid in corn for growth of chicks (Fernandez et al., 1994). Isoleucine is potentially limiting in low protein diets for laying hens that have been supplemented with lysine, methionine, and tryptophan (Jensen and Colnago, 1991; Keshavarz, 1997). Based upon these findings, isoleucine imbalance was readily precipitated by excessive dietary concentration of large neutral amino acids (histidine, methionine, phenylalanine, tryptophane, and tryrosine) in subsequent experiments (Park and Austic, 1998, 2000). Theoretically, any of the dispensable amino acids could be subject to imbalance, however, only hisitidine, isoleucine, lysine, methionine, threonine, and tryptophan have been used in the studies of amino acid imbalances.

OCCURRENCE OF AMINO ACID IMBALANCE

The effects of amino acid imbalances induced by disproportionate amounts of amino acids may depend on several factors such as methods of inducing imbalance, species and age of animal, and difference among optical isomers as imbalancing agents. The effects of amino acid imbalances range from a subtle decrease in the concentration of the most limiting amino acid in plasma to the complete and continued decrease of feed intake and growth rate in animals that can result in mortality.

Methodology to induce imbalance

Amino acid imbalances are most readily inducible in animals fed on diets having low dietary protein contents. Under conditions of low dietary protein, two approaches have been used. First, a relatively small amount supplement of one amino acid to the diet has been used. The supplementing amino acid was often a second-limiting amino acid. Secondly, a relatively large quantity of a mixture of amino acids lacking the limiting one can be used to induce imbalances. This second method usually causes a

severe growth depression in a more consistent and reproducible way than the former method. Frequently the mixture is composed of all indispensable amino acids except the one to be imbalanced.

Amino acid imbalances that might occur at adequate dietary levels of crude protein would be more interesting since low protein concentration seems unlikely to occur in practical conditions. In the studies of Davis and Austic (1982a, b) and Davis and Austic (1994), the control diet contained 20.6% crude protein that was adequate for growth of Leghorn chickens. A similar approach has been used to produce isoleucine imbalance using a 23.0% protein for broiler chickens (Park and Austic, 1998).

It could be worthwhile to determine the availabilities of amino acids in proteins used in basal diets in imbalance studies because the protein sources play an important role in the induction of amino acid imbalances. The proportion of natural and crystalline amino acids should also be controlled in order to manifest an amino acid imbalance in consistent manner in research on the metabolic and nutritional significance of imbalances in practical nutrition since free amino acids are more digestible than protein-bound amino acids.

When an imbalance is produced experimentally, a mixture of amino acids or an excessive amount of a single amino acid typically replaces an equivalent portion of the carbohydrates in the diet. Therefore, the final concentration of dietary crude protein will in most cases be higher in the imbalanced diet and the ratio of the dispensable to dispensable amino acids could be altered between the basal and imbalanced diets. It might be argued that the imbalanced group had a higher protein level, and the altered ration between the dispensable and the indispensable amino acids plays some role in depression of growth rate as well. In order to control this factor in studies of amino acid imbalance, two treatments could be made isonitrogenous by eliminating the difference in the concentration of dietary crude protein (Park and Austic, 1998, 2000).

Age of animal

It was reported that the activities of several enzymes involved in amino acid catabolism increased as animals matured (Waldorf et al., 1963), which means that mature animals have relatively higher capacities to degrade surplus amino acids than young animals. It seems a logical inference that mature animals are not as sensitive to amino acid imbalances as young animals. Accordingly, most studies in amino acid imbalances have applied the concept to immature animals including rats and chicks. Peng et al. (1975) reported that depression in feed intake and growth of rats that received histidine- or methionine-imbalanced diets were higher in young rats weighing about 105 g than in adult rats weighing about 298 g on average. From their studies, the susceptibility of the animals to amino acid imbalances appeared to vary directly with the extent of overall protein synthesis. Furthermore, the potential deleterious effects of excessive concentration of amino acids added to the diets is less likely to occur in the mature animals since the older animals would satisfy amino acid requirements in the normal diets in most cases. Therefore, modified procedures for experimental induction of amino acid imbalances may be required in studies of the mature animals.

Difference between optical isomers

Biological efficacies of D-amino acids as precursors of L-amino acids varies greatly among amino acids. L-forms of indispensable amino acids appear to be more potent for the induction of amino acid imbalances than D-forms (Harper et al., 1970). The D-isomers of lysine and threonine cannot replace the L-isomers for growth (Baker, 1986), whereas D-isomers of leucine and tyrosine had the same efficacy as the L-isomers (Robbins and Baker, 1977). D-isomers of methionine, phenylalanine, and valine showed from 70 to 90% of the efficacy of the L-isomers (Boebel and Baker, 1982a, b). The ketoacids of methionine, leucine, valine, isoleucine, and phenylalanine have been utilized well with efficacies ranging from 80% through to 100% of the L-amino acid. Their results indicate that some of hydroxyl analog of methionine, leucine, valine, isoleucine, and phenylalanine had the ability to substitute with varying efficiencies for L-amino acids.

BIOCHEMICAL AND NUTRITIONAL ASCPECTS OF AMINO ACID IMBALANCE

Feed intake

Feed intake was not considered as a significant physiological criterion in research on amino acid imbalance until Harper and Rogers (1965) suggested that a reduction in feed intake occurs prior to the depression of growth rate. One of the striking features, however, of amino acid imbalances is the occurrence of normal growth rate if the depression of feed intake is prevented. Several methods for stimulating feed intake in the imbalanced diet such as pair-feeding, force-feeding (Davis and Austic, 1982b), cold-temperature environment (Klain and Winders, 1964), insulin or cortisol injection (Noda et al., 1967), and finally infusion of limiting amino acid into the carotid artery (Tobin and Boorman, 1979) have resulted in normal feed intake, good growth and health. It is reasonable to conclude from these studies that a reduced feed intake is the cause rather than the result of the retardation in growth rate and that the main effects of amino acid imbalances may be manifested by way of feed intake regulation.

Growth rate

The growth retardation that occurs in amino acid imbalances always accompanies depressed feed intake in the laboratory rats and immature chickens. Park and Austic (1998) reported that weight gain and feed intake were decreased about 10% and 12%, respectively relative to the basal diet, when 5% imbalancing mixture was included in the diets marginally adequate in isoleucine.

Harper et al. (1970) indicated that the severity of amino acid imbalance might be less if the protein concentration of a diet is increased to an adequate level by natural sources of proteins because the amounts of limiting amino acid in the diet also are increased by this procedure. The protein concentration in the basal diet adopted by Park and Austic (1998, 2000) for the basal diet was enough for growth and maintenance. Therefore, it should be noted that chickens are sensitive to amino acid imbalance even when diets contain practical levels of protein, considering much of the research on growing rats has involved very low dietary levels of protein, ranging 6 to 7%.

There are some questions as to whether the depression of growth by amino acid imbalance is due solely to reduced feed intake. If reduced feed intake is the primary cause of decreased growth rate, the primary consequence of imbalances must be reflected in altered metabolic and physiological processes leading to the decrease in feed intake.

Feed selection

When rats are offered a choice between a protein-free diet and an amino acid imbalanced one, the animals select the former over the latter within a short period of time. This phenomenon was demonstrated in the case of threonine, histidine, and tryptophan imbalances (Pant, 1967). This is an interesting finding in view of the fact that a protein-free diet cannot support growth and eventually causes death, whereas an imbalanced diet is capable of supporting growth and sustaining life. Furthermore, when an imbalanced diet is corrected by supplementation of the limiting amino acid supplied, the rat selects the corrected diet over the imbalanced diet. There are some variations in feed selection responses since the preference for a protein-free diet or an imbalanced low protein diet depends on the severity of the imbalance.

Harper (1976) emphasized that the feed preference responses of the rat to an amino acid imbalance might be more sensitive than the feed intake responses. He explained the higher sensitivity of the feed preference responses in terms of survival value. In other words, feed preference responses may help an animal in the wild to select well-balanced amino acid patterns among the available feed in its environment.

Efficiency of nitrogen and limiting amino acid utilization

Fisher and Shapiro (1961) determined the body weight gain and carcass nitrogen content in broiler chicks fed lysine-imbalanced diets when they equalized the feed intake and therefore protein and limiting amino acid intake by adjusting dietary protein to energy ratio. They concluded that the imbalance diet did not affect the efficiency of utilization of the protein and of the limiting amino acid. Apparently, if feed intake is equalized between imbalanced and basal balanced groups, the efficiency of utilization of the limiting amino acid seems not to be decreased and might even in some cases be improved by the imbalance (Cieslak and Benevenga, 1984). However, in the study of Park and Austic (1998), the efficiency of isoleucine utilization for growth (grams of weight gain per milligram of isoleucine intake) was decreased when isoleucine imbalanced diet precipitated with a mixture of 5% imbalancing amino acids.

It is generally accepted that crystalline free amino acids are absorbed more rapidly than protein-bound amino acids (Rolls et al., 1972). By use of a once a day feeding regime, Patridge (1985) demonstrated that imbalances might be induced at the tissue level by the lack of synchrony in absorption between amino acids from crystalline and protein-bound sources. Under these conditions, growth rate and efficiency of utilization of dietary nitrogen and limiting amino acid would be depressed, but these effects can be prevented by more frequent feeding.

Adaptation

In view of the extensive research leading to the development of the concept of amino acid imbalances, relatively little attention has been given to the study of adaptation of animals to amino acid-imbalanced diets.

There is evidence that depression in growth and feed intake is no longer prominent after a few days of offering imbalancing diets to rats (Davis and Austic, 1994). Tews et al. (1980) reported that the concentration of the most limiting amino acid in plasma in rats fed imbalanced diets decreased significantly within one day of supplying the imbalanced diets, but were no longer significantly decreased after 5 days.

The mechanism of adaptation to amino acid imbalances in rats is not clear since it could be a metabolic adaptation or an adaptation in regulatory systems for feed intake. In order to test these possibilities, Leung and Roger (1987) demonstrated that the adaptation was accelerated when they made lesions in brain sites such as the hippocampus and the septum. In addition to brain areas implicated in the adaptation for amino acid imbalance, Bellinger et al. (1994) suggested that the liver played a role in the adaptation. This was based upon their observation of increased feed intake in

rats fed a severely isoleucine imbalanced diet when their livers were completely denervated.

In contrast to these findings in rats, no outstanding adaptive responses of feed intake, changes in the concentration of most limiting amino acid in plasma, and activities of enzyme involved in the catabolism of a limiting amino acid were observed in chicks fed a threonine-imbalanced diets for 6 days (Davis and Austic, 1994). As well, it appears likely that broiler chicks did not adapt to the imbalanced diet since the depressed feed intake and growth rate and alterations in plasma isoleucine and hepatic BCKAD activity persisted through 13 days of experiment (Park and Austic, 1998).

Effect of previous diet

In a study of diet selection in rats offered a choice between a protein-free and an imbalanced diet, rats that had previously received a high protein diet preferred an imbalanced diet (Leung et al., 1968). Rats fed an imbalanced diet showed the lowest feed intake when offered a low protein diet prior to the start of experiment (Peng and Harper, 1969). Therefore, the previous diet may account for the variability in the effects of amino acid imbalances among different researchers. It is possible that the protein level of the diet affects the rate of amino acid-catabolism and that this, in turn, determines the responses to amino acid imbalanced diets.

Limiting amino acid concentrations in the tissues

The pattern of plasma amino acids in animal fed a diet imbalanced in a specific amino acid resembles that of animal fed a diet severely deficient in that amino acid. Three attempts have been undertaken to explain the mechanism for the decreased plasma concentration of the limiting amino acid due to amino acid imbalances.

First attempt was proposed by Salmon (1954). He suggested that the catabolism of a limiting amino acid increased consistently with enhanced catabolism of the surplus amino acids that were included in the diet to cause an amino acid imbalance. This hypothesis has received little attention because conflicting reports on whether differences in $^{14}CO_2$ production from ^{14}C-labeled amino acid were observed in animals fed balanced and imbalanced diets (Peng and Evenson, 1979; Soliman and King, 1969). It is questionable that the measured parameters of metabolic changes would remain for a longer period of time and be entirely responsible for the depressed plasma concentration of the limiting amino acid since most of the measurements were made in the range from 1 h to 12 h after feeding the labeled diets.

Harper et al. (1964) hypothesized that imbalancing amino acids stimulate protein synthesis in liver, thereby depleting plasma limiting amino acid. This hypothesis is later supported by several investigators who reported increases in hepatic polysomal aggregation or incorporation of labeled amino acids into liver protein of animal fed an imbalanced diet (Ip and Harper, 1974; Esteve-Garcia, 1984). However, the specific activities of amino acids in precursor pools in liver protein were not determined, and changes of protein degradation in liver were not determined. Also, their studies have focused on metabolic changes at the early stage of amino acid imbalances, thus it is difficult to affirm an actual increase of net protein synthesis in liver from these data.

Peng et al. (1972) observed that the concentration of limiting amino acid, threonine decreased more rapidly in brain than in plasma when they induced a threonine imbalance. The concentration of amino acids supplemented to cause the imbalance increased in plasma rather than in brain after just 3 h of feeding imbalanced diets. There are some reports that the increased concentration of the limiting amino acid in tissues was not caused by inhibition of the intestinal absorption of the limiting amino acid. It was then proposed that competitive transport of amino acids plays an important role in the decrease of the limiting amino acid concentration in tissues such as brain. It was reasonable to suppose that because of their higher plasma concentrations, the amino acids supplemented to induce an imbalance can be transported more dominantly from plasma to tissue, especially brain, than the imbalanced amino acid in plasma. This is because the blood-brain barrier is believed to contain saturable transporters specific for groups of chemically and structurally related amino acids. Tews et al. (1979) found a decreased concentration of threonine in the brain of rats fed a diet imbalanced in threonine by supplementation of the diet with an amino acid mixture containing serine, glycine, and alanine. These four amino acids share a common transport system for small neutral amino acids (SNAA) and threonine can be transported by carriers for SNAA and large neutral amino acid (LNAA). However, the complexity of transport systems at the blood-brain barrier was demonstrated using the basic amino acids, ornithine, lysine, and arginine that do not share a common transporter with threonine. These amino acids could induce a threonine imbalance (Tew et al., 1979). Davis and Austic (1982a) observed that 0.9% addition of phenylalanine to the diet did not precipitate a threonine imbalance. Phenylalanine is know to share common transporters with threonine.

Enzymes involved in amino acid imbalances

If amino acid catabolism has a role in amino acid imbalances, then an increase in activity of enzymes responsible for the degradation of the first limiting amino acid should be evident in imbalances. For example, branched-chain α-keto acid dehydrogenase (BCKAD),

which regulates the irreversible degradation of branched-chain α-keto acids is believed to be the primary regulated enzyme of branched-chain amino acid catabolism (Harper et al., 1984). The BCKAD is inactivated by a kinase that, in turn, is allosterically controlled by the concentration of branched-chain α-keto acid and possibly certain other keto acids (Paxton and Harris, 1984). Because the precursor amino acids are usually present in imbalancing mixtures of amino acids, isoleucine imbalance were due in part to increased BCKAD activity, leading to the decreased plasma isoleucine concentration and the increased isoleucine requirement of chicks under conditions of isoleucine imbalance (Park and Austic, 1998).

NEURAL MECHANISM IN AMINO ACID IMBALANCES

Leung and Rogers (1969) were the first to examine the role of the brain in recognizing the imbalances. They observed that the depressed feed intake of rats fed an imbalanced diet could be restored by the infusion of a small amount of the most limiting amino acid into the carotid artery a few hours before feeding the imbalanced diet, whereas a similar amount of the same amino acid infused into the jugular vein had no effect on feed intake. This study suggests that the concentration of limiting amino acid in blood supplying the brain determines the feed intake changes in animals fed amino acid imbalanced diets.

Gietzen (1993) summarized research on amino acid imbalance indicating that the concentration of limiting amino acid was found to be decreased in specific sites of brain, such as the anterior prepyriform cortex, anterior cingulated cortex, locus ceruleus, and nucleus of solitary tract among 14 microdissected brain areas when an imbalanced diet was fed to rats.

Evidence for the role of the anterior prepyriform cortex in the imbalances is provided by the study of Beverly et al. (1991) in which the consumption of a threonine-imbalanced diet was increased in rats by the injection of 2 nmol threonine into the prepyriform cortex. Injection of 4 nmol into the prepyriform, however, did not result in a significant increase of feed intake even though both injections of threonine into the prepyriform of rats reversed their selection of a protein-free diet in favor of a threonine-imbalanced diet. It can be said that the presence of the limiting amino acid in the prepyriform exerts its effects separately on dietary selection and on quantitative intake of an imbalanced diet, depending on the dose level of the limiting amino acid. It would thus appear that the anterior prepyriform cortex is important in the initial recognition of amino acid imbalances.

The possibility that amino acid imbalances causes impaired synthesis of neurotransmitters was raised by Harper et al. (1970). Gietzen et al. (1986) observed that the concentration of norepinephrine in the prepyriform of rats was decreased by feeding amino acid imbalanced diets. They speculated that specific neurotransmitters had a role in the regulation of feed intake in response to ingestion of imbalanced diets. In other studies, however, the effects of amino acid imbalances were not associated with changes of specific neurotransmitters in brains of rats (Tackman et al., 1990) and chicks (Harrison and D'Mello, 1987). Thus, the role of neurotransmitters in the prepyriform cortex in the recognition of amino acid imbalances needs further studies.

CONCLUSION

The question as to whether the requirement of the most limiting amino acid is affected by amino acid imbalances is worthy of review, especially as regards the method of expressing amino acid requirement. A common procedure to create imbalances in which the levels of all amino acids other than one amino acid tested in the diet are increased was used by several investigators. All studies demonstrated that the requirement of the limiting amino acid increased with increasing dietary protein concentration. This means that the content of the first limiting amino acid in the corrected diet should be increased to correct an amino acid imbalance and the concentration of the limiting amino acid in an imbalanced diet must be higher than that of a basal balanced diet in order to obtain a growth rate equivalent to that obtained using the basal balanced diet.

The actual amount of feed intake, and consequently the limiting amino acid intake, decreases to various extents when animals were fed imbalanced diets, depending on the degree of imbalance. This means that the quantity of the limiting amino acid consumed does not necessarily have to be increased to sustain a given rate of growth. In fact, the relationship between amino acid intake and growth rate is similar for animals fed basal diets and the same diet to which imbalancing mixtures of amino acids have been added.

According to D'Mello (1990), amino acid imbalances do not decrease the efficiency of limiting amino acid utilization or increase the requirement of the limiting amino acid. He carried out the trials with three basal diets, a balanced diet (22.5% crude protein), a moderately lysine-imbalanced diet, and severely lysine-imbalanced diet (31.5% crude protein), which were prepared by adding imbalaning mixtures at the expense of glucose. Each basal diet was supplemented with graded level of lysine. Interestingly, he observed as highly significant linear relationship between lysine intake (mg lysine per day) and weight gain with a single response curve made with all data points of three diet treatments. He could remove the effects of difference in feed intake of three groups by expressing

the relationship of amino acid and weight gain as the intake of limiting amino acid per day versus weight gain, in contrast to percentage of the limiting amino acid in the diet versus weight gain.

Nevertheless, it should be emphasized that the degree of feed intake in the case of amino acid imbalances bears an important and practical implication for a commercial production of animals since the feed intake decrease can potentially lead to enormous losses in profits due to low growth rate. In this regard, Wethli et al. (1975) suggested that amino acid imbalances might occur in diets based upon conventional ingredients like low-quality oilseed meals. Also, according to the survey of Hendricks et al. (2004), there is large variation of amino acid quality in meat and bone meal by rendering methods. In these cases supplementation of the limiting amino acids could be beneficial in preventing the decrease of feed intake that could otherwise occur as a result of amino acid imbalance (Hsia, 2005). In conclusion, it can be said that higher concentration of a potentially limiting amino acid should be recommended for the diets composed of ingredients that might cause some amino acid to be imbalanced.

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