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## Nutrition and Coccidiosis

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### Introduction

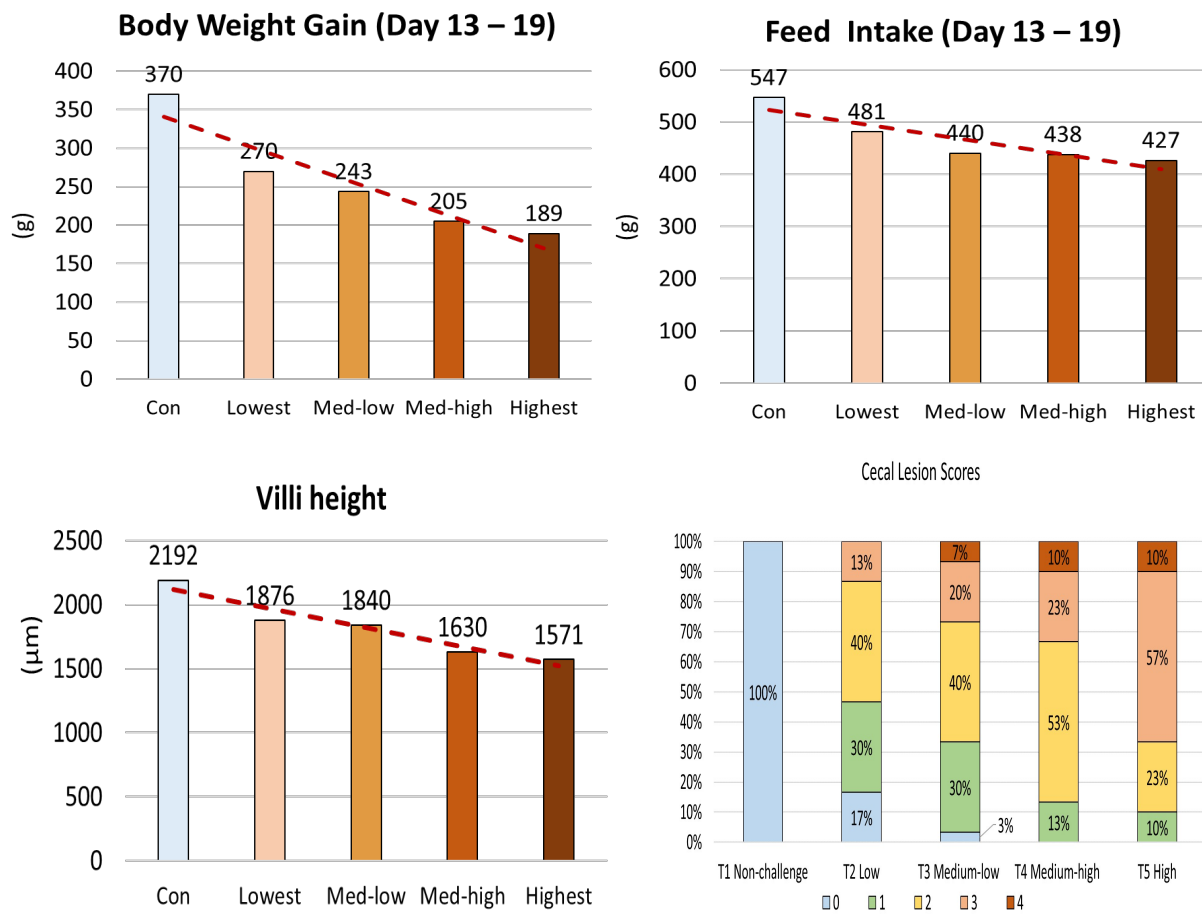
Coccidiosis is the most common parasitic disease caused by *Eimeria* spp., leading to over \$14 billion economic loss worldwide annually (Blake et al., 2020). The most prevalent *Eimeria* spp. in poultry include *E. tenella*, *E. maxima*, *E. acervulina*, *E. brunetti*, *E. necatrix*, *E. praecox*, and *E. mitis* and have different level of pathogenicity and specific infection sites in the intestine (Cervantes et al., 2020). *Eimeria* spp. invade intestinal epithelial tissues and induce intestinal damage, causing inflammation, oxidative stress, hemorrhage, and diarrhea. Furthermore, coccidiosis causes reduction of growth performance, intestinal integrity, nutrient digestibility, and increase of mortality and mobility in poultry.

Nutrition strategies have been evaluated to mitigate detrimental impact of coccidiosis in poultry. Prebiotics, probiotics, enzymes, antioxidants, amino acids, vitamins and minerals have shown to reduce severity of intestinal damage and stimulate nutrient digestion and fast recovery of the intestinal damage and growth performance (Parker et al., 2007; Amerah and Ravindran, 2015; Bortoluzzi et al., 2018; Oxford and Selvaraj, 2019; Souza et al., 2020; Yadav et al., 2020; Castro et al., 2020ab; Teng et al., 2020a). In order to develop efficient nutrition strategies, understanding of *Eimeria* infection on gut health and nutrient digestibility is critical. Thus, this paper will discuss about 1) *Eimeria* infection on gut health; 2) *Eimeria* infection on nutrient digestibility; and 3) Roles of key amino acids in *Eimeria* challenged broilers.

### Eimeria infection on gut health

*Eimeria* infection increases intestinal damage, lesion score, gut permeability, inflammation, and oxidative stress, and such detrimental effects are highly correlated with

*Eimeria* oocysts ingested by chickens (Adedokun and Adeola, 2016; Rochell et al., 2016; Zhang et al., 2017; Sakkas et al., 2018; Teng et al., 2020b, 2021). Recently, Teng et al. (2020b) evaluated graded levels of mixed *Eimeria* challenge (*E. maxima*, *E. tenella*, and *E. acervulina*) on growth performance and gut health (gut permeability, intestinal morphology, lesion score, and intestinal tight-junction protein expression) in broilers. The authors found that increase of *Eimeria* challenge dose linearly reduced feed intake and body weight gain, and intestinal villi height (Fig. 1), whereas it increased lesion score and upregulated key tight junction proteins, claudin 1 and Jam2. Moreover, gut permeability linearly increased on 5-, 6-, and 7-days post-infection (dpi) when *Eimeria* oocysts challenge dose increased. However, the gut permeability was back to the normal on 9 dpi. The results indicate that *Eimeria* infection causes detrimental effects on growth performance and gut health.

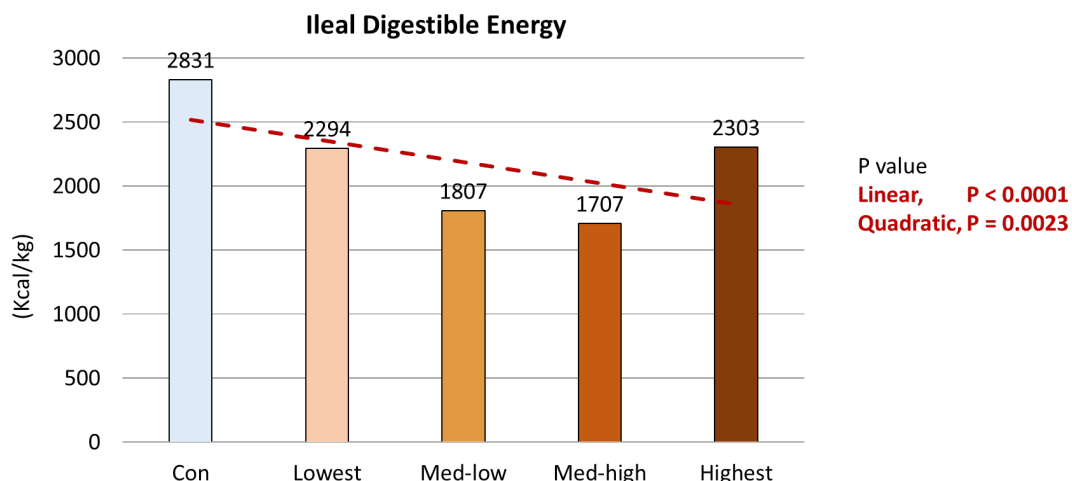


**Figure 1.** Effects of graded *Eimeria* challenge on growth performance and lesion score (Teng et al., 2020b).

### Eimeria infection on nutrient digestibility

Several studies have shown that *Eimeria* infection reduces nutrient digestibility (Persia et al., 2006; Sakkas et al., 2018; Rochell et al., 2016; Teng et al., 2020b, 2021). Rochell et al (2016) reported that the apparent ileal digestibility (AID) of amino acids, except tryptophan and glycine, was linearly reduced in response to graded *E. acervulina* challenge. A study by Teng et al. (2020b) showed that increased mixed *Eimeria* spp. infection linearly decreased AID of digestible energy (Fig. 2) and minerals, such as sodium, potassium, calcium, magnesium, and phosphorus. These results clearly show that *Eimeria* infection reduces nutrient digestion and absorption in broilers, resulting in growth performance loss.

The reduction of nutrient digestibility caused by *Eimeria* infection may be due to reduction of digestive enzyme secretion and nutrient transports expression in the intestine. It has been reported that the activity and expression of several key mucosal brush border enzymes, such as maltase, sucrose, aminopeptidase, sucrose isomaltase, and alkaline phosphatase, were considerably limited by *Eimeria* infection in the intestine of broilers (Adams et al., 1996; Paris and Wong, 2013; Su et al., 2015). In addition, *Eimeria* infection significantly inhibits the expression of nutrient transporters in the intestine (Su et al., 2014, 2015; Teng et al., 2021). *E. acervulina* and *E. maxima* reduced the expression of glucose transporters as well as amino acid transporters including neutral amino acid transporters, cationic amino acid transporters, and excitatory amino acid transporters in the intestine of broilers (Su et al., 2015). Teng et al. (2021) also reported that graded *E. maxima* infection linearly regulated glucose and amino acid transporters in the brush boarder and basolateral member of the intestine.



**Figure 2.** Effects of graded *Eimeria* challenge on ileal digestible energy (Teng et al., 2020b).

### **Roles of key amino acids in *Eimeria* challenged broilers**

It has been reported that specific amino acids exhibit beneficial effects on intestinal development, immunity, gut integrity and anti-oxidant defense system in broilers challenged with *Eimeria* spp. (Gottardo et al., 2016; Zhang et al., 2017; Bortoluzzi et al., 2018; Castro et al. 2020ab). Among key amino acids, the functional effects of methionine, threonine, glutamine, and arginine have gained attention to alleviate detrimental effects of *Eimeria* infection in broilers.

Methionine is the first limiting amino acid in corn and soybean-based diets for poultry and plays important roles in metabolic functions, including methyl group donors, sulfur donors, and formations of cysteine, glutathione (GSH), taurine, carnitine, and polyamine (Stipanuk, 2004; Bunchasak, 2009). Because *Eimeria* infection reduces methionine digestibility and increases oxidative stress and inflammation in the body (Persia et al., 2006; Rusell et al., 2016; Souza et al., 2020; Yadav et al., 2020; Teng et al., 2021), methionine supplementation may improve anti-oxidant defense via GSH and reduce oxidative stress. Chen et al. (2013) reported that methionine supplementation increased serum SOD activity and total antioxidant potential in broilers and turkeys (Chen et al., 2013; Jankowski et al., 2017). Castro et al. (2020a) found that methionine supplementation increased GSH in the liver of broilers infected with three *Eimeria* spp. (*E. acervulina*, *E. tenella*, and *E. maxima*), alleviating oxidative stress caused by *Eimeria* infection.

Threonine is the third limiting amino acid and the major component of mucin in the intestine (Corzo et al., 2007; Faure et al., 2002). Because *Eimeria* infection causes intestinal damage and increases mucin production in the intestine, threonine is one of the important amino acids to maintain intestinal integrity and rapid recovery during and after *Eimeria* infection. Zhang et al (2017) reported that threonine deficiency significantly increased *Eimeria* oocysts shedding and gut leakage in 25X *Eimeria* vaccine challenged broilers, and increased supplementation of threonine from 0.48 to 0.96% improved intestinal integrity and reduced oocyst shedding. Kidd et al. (2003) also reported that increased threonine supplementation from 0.6 to 0.8% enhanced growth responses (body weight gain, feed intake, and feed conversion ratio) in broilers, regardless of mid-*E. acervulina* challenge (30,000 oocysts). Recently, Teng et al. (2021) found that 0.75% threonine supplementation in a low protein diet increased villus

height and JAM2, a tight junction protein, in broilers challenged with mixed *Eimeria* spp. (*E. acervulina*, *E. maxima*, and *E. tenella*), suggesting that threonine supplementation can be a nutritional strategy to improve gut health in broilers under coccidiosis condition. Moreover, threonine is a critical amino acid regulating immunoglobulin production and inflammatory responses. Increasing dietary threonine enhanced IgA secretion and reduce pro-inflammatory cytokines such as INF- $\gamma$  and IL-1  $\beta$  (Chen et al., 2017).

Glutamine is an important fuel source of enterocytes during cell proliferation and repairment particularly during inflammation, oxidative stress and challenge conditions and a key component of glutathione that plays an essential role in body antioxidant system (Rao and Samak, 2012; Bortoluzzi et al., 2018). It has been reported that dietary supplementation of glutamine improved growth performance and gut health in broilers (Yi et al., 2005; Waldroup et al., 2012; Luquetti et al., 2016; Oxford and Selvaraj, 2019). Yi et al. (2005) reported that 1% glutamine supplementation improved growth performance and intestinal development in broilers challenged with 40,000 oocysts of *E. maxima*. Oxford and Selvaraj (2019) also found that 1% glutamine supplementation increased villus height and villus height to crypt depth ratio and the gene expression of tight junction proteins, whereas there was no difference in growth performance among the treatments. Recently, Teng et al. (2021) reported that 0.75% glutamine supplementation in a low protein diet reversed detrimental effects of *Eimeria* infection on tight junction protein expression in broilers.

Arginine is an essential amino acid for poultry and has beneficial effects on body composition (fat, muscle, and bone metabolisms), oxidative stress, immunity, and gut health in poultry. Besides the muscle protein synthesis, arginine is an essential precursor of many key molecules in the body such as glutamate, glutamine, creatine, nitric oxide, proline, and polyamines (Ball et al., 2007; Khajali and Wideman, 2010; Castro et al., 2019). Moreover, arginine plays an important role in growth hormone (GH) secretion and consequently increases insulin-like growth factor (IGF-1), which regulates muscle accretion and bone development (Liu and LeRoith, 1999; Corzo et al., 2003; Silva et al., 2012). In addition, it was reported that an abdominal fat deposition was limited in broilers fed additional arginine supplemented diet (Fouad et al., 2013). Dietary supplementation of arginine improved total body antioxidant capacity and increased key antioxidant system in the body, including glutathione and superoxide dismutase (Atakisi et al., 2009; Duan et al., 2015).

Eimeria infection significantly affects arginine metabolism in broilers; *E. acervulina* infection reduced plasma arginine and increased nitrogen oxide production via arginine degradation (Allen and Fetterer, 2000; Rochell et al., 2016). Arginine supplementation reduced oocysts shedding of Eimeria spp. (Allen 1999; Laika and Jahanian, 2017), suggesting that arginine may directly and indirectly influences Eimeria life cycle. Recently Teng et al. (2021) reported that dietary arginine supplementation in broilers fed a low protein diet significantly reduced gut permeability, indicating that arginine supplementation can be a nutritional strategy to improve gut health under coccidiosis condition. Castro et al. (2020b) evaluated the effect of different levels of arginine (1.04, 1.14, 1.24, 1.34, and 1.44%) on growth performance and gut health of broilers challenged with mixed Eimeria spp. Eimeria challenge adversely affected growth performance, intestinal integrity, and nutrient digestibility in broilers. The birds fed 1.44% arginine had significantly higher body weight gain compared to those fed 1.04%, and 1.34% arginine fed birds showed lower feed conversion ratio compared to those fed 1.04%. Moreover, the 1.34% arginine group had significantly higher the expression of the tight junction protein Zonula occludens-1 (ZO-1) at 6 days post-infection (dpi), whereas the 1.44% arginine group had the highest expression of ZO-1 and ZO-2 at 14 dpi, indicating that dietary arginine supplementation has positive effects on gut health in broilers under coccidiosis condition.

### **Summary**

Coccidiosis is a common enteric disease caused by Eimeria species; it considerably reduces growth performance, nutrient digestibility, intestinal integrity, and gut health and increases mortality and economic loss for the poultry industry. Thus, nutrition strategies, such as supplementing pre- and probiotics, amino acids, and feed additives having anti-oxidant and anti-inflammatory properties, would improve growth performance and gut health in poultry. Moreover, precise determination of nutrient digestibility and requirements/functions of key amino acids under coccidiosis are essential to develop nutritional strategies to improve growth performance and alleviate negative effects of Eimeria infection in poultry.

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