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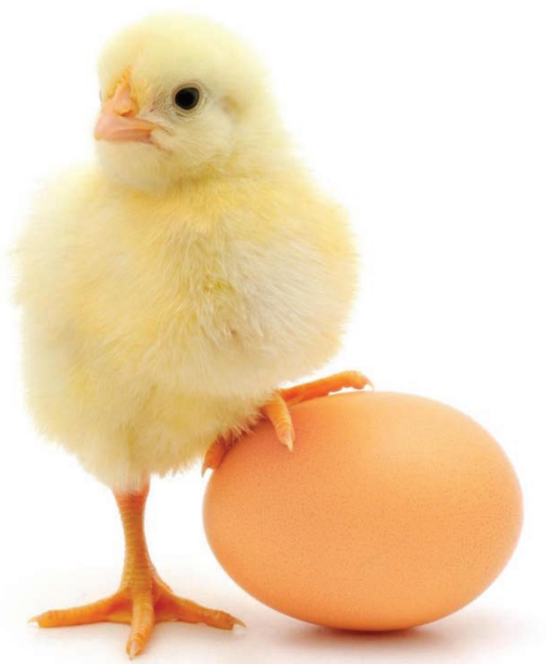

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# Review Article
# Heat Stress and Gut Microbiota: Effects on Poultry Productivity

[1]Fisayo T. Akinyemi, [2]Semiu F. Bello, [3]Victoria A. Uyanga, [4]Charles Oretomiloye and [1]He Meng

[1]Shanghai Key Laboratory of Veterinary Biotechnology, School of Agriculture and Biology, Shanghai Jiao Tong University, Shanghai, 200240, China
[2]Department of Animal Genetics, Breeding and Reproduction, College of Animal Science, South China Agricultural University, Guangzhou, People's Republic of China
[3]Shandong Provincial Key Laboratory of Animal Biotechnology and Disease Control and Prevention, Shandong Agricultural University, No. 61 Daizong Street, Tai'an City, Shandong Province, 271018, China
[4]Department of Nutrition and Dietetics, Obafemi Awolowo University, Ile -Ife, Osun State, Nigeria

## Abstract
The gut microbiota has been extensively examined because it plays pivotal roles in poultry health, growth and development. In poultry flocks, gut microbiota and host health and productivity are interwoven and influenced by factors including host derived, environmental and nutritional factors, which consequently influence the growth and performance of these birds. The responsiveness of chickens' gut microbes during stress conditions such as heat stress that is commonly encountered during production is of imminent concern because healthy maintenance of the host-gut-microbiota relationship will result in improved bird growth and productive performance. Previous studies have established the link between gut microbiota alterations and immune system dysfunction in poultry birds, which is primarily initiated by stressors. However, shifts in the gut microbiota could also be linked to several diseases that negatively affect the immune system. The goal of this mini review was to focus on understanding the impact of heat stress on the gut microbiota and how this affects the health of the birds. We also suggest possible ways to ameliorate stress in poultry for improved productivity. Good knowledge of these salient points would help to develop new approaches to provide a better environment and feeding conditions for poultry birds, as strategies toward achieving improved poultry production.

Key words: Heat stress, gut microbiota, poultry health, poultry productivity, gut health, immune system

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Corresponding Author: He Meng, Shanghai Key Laboratory of Veterinary Biotechnology, School of Agriculture and Biology, Shanghai Jiao Tong University, Shanghai, 200240, China



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Data Availability: All relevant data are within the paper and its supporting information files.

## INTRODUCTION

Heat stress poses a major threat to the poultry industry and has negative consequential effects on the immune system, production, and the health and well-being of poultry birds[1-3]. Heat stress affects global poultry production by reducing feed consumption, egg production and quality and increasing the mortality rate of laying hens, which adversely influences intestinal growth and development and leads to decreased nutritional digestibility[4-8]. Heat stress occurs when the heat produced in animal body exceeds its dissipation capacity and the body becomes unable to get rid of excess heat[9]. Nearly all species respond to heat stress but poultry birds are extremely vulnerable temperature-related stress. Poultry birds react differently to high temperatures depending on the duration and amount of heat stress[10]. They undergo thermal homeostasis under environmentally stressful situations, which results in an increase in the breathing rate that causes the body to enter oxidative stress[11].

The hen undergoes different physiological and environmental stresses during the hatching process, which also influences the gut microbiota composition[12]. In poultry birds, the gastrointestinal tract (GIT) encompasses microbial communities that essentially function in gut homeostasis and host metabolism as well as the animals' physiology, production and health[13]. Heat stress has been shown to alter the composition and population of microbiota in chicken intestines[14-16]. Additionally, it allows for proliferation of bacteria that are pathogenic such as *Escherichia coli*, *Salmonella* and total aerobic bacteria in the cecum microflora[17]; there is also an increasing abundance of zoonotic pathogens such as the family Moraxellaceae and order Pseudomonadales in the jejunum and order Rickettsiales in the cecum[18]. Heat stress can result in gut dysbiosis because the intestinal tract of poultry birds is highly susceptible to stressors, which can lead to intestinal mucosal damage, alterations and upset of the defensive microbiota[19,20].

While the impact of heat stress on poultry production has been well reviewed[2,9,21-23], much less has been documented concerning its effects on the gut microbiota and host health. It is imperative to understand the association of heat stress with the gut microbiota and its implications on poultry health and production performance. To aid our understanding, we reviewed published studies covering aspects of heat stress in poultry birds, the impact of heat stress on gut microbiota and its composition, the role of gut microbiota in host health and measures to alleviate heat stress to improve proper functioning of gut microbes.

**Role of the gut microbiota in host health:** A fundamental part of a functioning ecosystem is the gut microbiota, which interrelates and benefits its host at various multifaceted levels to achieve a mutual association[24]. The interactions between the host and the microbiota is a symbiotic relationship that is vital to poultry well-being, health and production[25,26]. Thus, the interactions must be balanced within the intestinal mucosa to maintain a healthy gut, which translates into a healthy animal[24]. One of the major protective components in the chicken GIT against enteric and harmful pathogens is the gut microbiota[27]. Disturbance of the gut microbiota in poultry has been considered to be a major cause of bacterial infection in chicks[28]. Gut microbiota has a noteworthy impact on host health[29] and productivity[30] and it serves as an essential mediator of host health[31]. For example, the intestinal microbiota plays a substantial role in normal host physiology, maintaining immune metabolic homeostasis and protecting the host against pathogens[32,33].

The microbiota plays a prominent role in the control of the gut-brain axis, especially when the body system is stressed[34]. During acute stress, the gut microbiota contributes to the innate immune system recovery after the animal is stressed[35]. In animals, research has shown that the gut microbiota strongly influences nutrient metabolism and the maintenance of homeostasis[14], thereby mediating the pivotal link between health and disease. These microorganisms also interact with several organs and systems in the body, including neurological, respiratory, digestive, skeletal and cardiovascular system[36] and they have the capability to produce nutrients from remnants that host cannot digest[37]. A balanced gut microbiota is involved in a broad metabolic range of activities that is of great advantage to the host[38].

The health status of animals and their nutrient uptake are largely determined by gut health, which is influenced by both the gut microbial flora and the host immune functioning system[39]. The effects of the gut microbiota on immune system development cannot be overemphasized and it has some likely implications on sound health and productivity[40]. Intestinal microbial establishment and development of immune fitness are interwoven and both are affected by early-life stressors such as environmental and management stress[41].

**Impact of heat stress conditions on gut microbiota composition:** The GIT is an organ that is most affected by heat stress[42]. The balance of gut beneficial bacteria is essential for a healthy intestinal microbiome and associated physiological homeostasis. Imbalance of gut microbes might be attributed to heat stress, especially during nutrient competition between the host and harmful bacteria[43].

A previous study revealed that heat stress tends to decrease cecal *Lactobacilli* counts while increasing *Clostridia* populations in poultry[16]. Beneficial bacteria including *Lactobacilli* and *Bifidobacteria* in poultry are depleted during heat stress[15], suggesting that their role against pathogen colonization may be impaired, which enhances gut susceptibility to enteric pathogen invasion and colonization[44]. Further analysis observed that during heat stress in birds, decreased similarity coefficients of bacterial communities occurs, which suggests an increased variability in intestinal barrier composition rather than enrichment of the amount of bacterial diversity[15]. Similarly, in ducks, microbiota composition differs significantly between the jejunum and cecum during heat stress[18]. The cecal composition of the gut microbiota was markedly affected during heat stress with changes at the phyla and genus levels. The relative abundance of *Firmicutes*, *Proteobacteria* and *Tenericutes* were increased, while that of *Bacteroidetes* and *Cyanobacteria* decreased. Genus level changes involved *Bacteroides* as the most dominant species, which was followed by *Oscillospira* and *Faecalibacterium*[20]. Table 1 shows the summary of the effect of heat stress conditions on gut microbiota populations (Table 1).

Moreover, the gut segments have been described as responding differentially in susceptibility to heat stress, with the most severe effect was on the ileum[45]. Broilers exposed to cyclic heat stress at 33°C for 10 h daily had lower viable *Lactobacillus* and *Bifidobacterium* counts and improved coliform and *Clostridium* viable counts in the small intestinal contents[16]. During heat stress conditions, alterations to the intestinal epithelial barriers resulting dysfunction (or "leaks")[46] that allows permeation of endotoxins, luminal antigens and bacteria reaching the bloodstream[47]. The derived endotoxins from the gut and pathogenic bacteria are implicated in morbidity and mortality[48]. Similarly, because oxidative stress is induced after heat stress, the interaction between the mucosa and microbes or microbial toxins triggers the severity of oxidative stress, which leads to coccidiosis caused by *Eimeria*. Coccidiosis caused by *Eimeria* is one of the most common poultry diseases. It is parasitic in nature and destroys the intestinal epithelial barriers, promoting nutrient malabsorption during oxidative stress[49].

Taken together, heat stress exposure leads to microbe instability and the bacterial translocation[1], which impacts behavior, immune response and the physiological parts of animals and humans[9,50]. The production rate in poultry can be adversely affected because of physiological changes that are caused by chronic heat stress[51]. Extensive studies have revealed the impact of stress on gut microbiota composition and stability, which is unfavorable to chicken health, welfare and the poultry industry[16,18,45]. Important measures must be implemented to improve the resistance of poultry birds to heat stress because the inability to curb this detrimental situation will result in repeated disruption of the gut microbial population, which enhances the continuous decline in productivity.

**Measures to alleviate heat stress to improve gut microbes in poultry production:** Heat-stress is a major environmental stressor in poultry production globally because of increasing global temperatures and its associated effects of compromising physiological composition, microbiology and the immune system, which results in anomalies and poor performances in poultry[9,52]. It is necessary to understand and regulate heat stress conditions in poultry farming because of their influences on successful production. To combat the impact of heat-stress in poultry birds, poultry farmers need to adopt the measures that are described below.

**Genetic manipulation:** Multiple interrelated factors influence the development, composition and population of the host gut microbiota, with host genetics playing a significant but ambiguous, role[53,54]. The microbial flora in the gut are acquired before birth and it is then developed and shaped dynamically after birth into complex physiological networks with environment and dietary factors influencing the abundant diversity of microorganisms that are developing within neonates[55]. The uncertainty encountered in clearly defining the influence of host genetics on gut microbiota stems from the interaction between environmental and host genetics including factors such as age, environmental conditions, genetic distance and population variation[56], as such overlapping the direct effects of host genetics on gut microbiota confirm under controlled environmental conditions. The host genetic background is responsible for a sizable amount of microbial abundance in the gut[57].

Heritability studies on gut microbiotas revealed that host genetics may be partly responsible for genetically determining the abundance of a subclass of microbes[58]. This shows the significant contribution of host inheritance in early development of the gut microbiota, thus highlighting the influence of animal breeding on gut microbiota. Future studies to identify the host-microbe-metabolite interactions and demonstrate the functions of host genetics in determining gut microbiota composition are required[59].

**Environmental modification strategies:** Poultry birds lack sweat gland, which makes them very sensitive to heat stress[60] and the use of non-evaporative (radiation and convection) heat dissipation is highly important. The

Table 1: Impacts of heat stress conditions on gut microbiota populations in poultry species

| Poultry species | Heat stress condition | Experimental diets | GIT segment | Gut microbiota population changed with heat stress: Enriched | Gut microbiota population changed with heat stress: Decreased | References |
|---|---|---|---|---|---|---|
| Broilers | CT (24 to 26°C) vs HS (34-38°C) for 28 days | Standard diets | Caecal contents | *Firmicutes*, *Tenericutes* and *Proteobacteria*, *Anaeroplasma* and *Lactobacillus* phyla | *Bacteroidetes* and *Cyanobacteria* phyla; *Bacteroides*, *Oscillospira* *Faecalibacterium* and *Dorea* genera | [20] |
| Broiler chick | CT (21±1°C) vs HS (31±1°C) from 28-42 day old | Standard diets | Ileal contents | *Clostridium* XIVb, *Streptophyta*, *Faecalibacterium*, *Rothia*, *Alistipes*, *Azospirillum* and *Oscillibacter* | *Coprococcus* and *Streptococcus* | [14] |
| Ducks | CT (25°C) vs HS (32°C) for 8 h day$^{-1}$ for 3 weeks | Standard diets | Jejunum, Ileum and Cecum contents | *Proteobacteria* (phylum), *Pseudomonadales* (order), *Moraxellaceae* (family), *Acinetobacter* (genus) and *Mitochondria* (genus) in jejunum *Rickettsiales* (order) and *Mitochondria* (family) increased in caecum | *Firmicutes* (phylum), *Bacilli* (class), *Lactobacillales* (order), *Lactobacillaceae* (family) and *Lactobacillus* (genus) in jejunum *Negativicutes* (class) and *Selenomonadales* (order) in caecum | [18] |
| Laying hens | Minimum temperatures (25.2-29.4⁻C) vs maximum temperatures (29.6-34.1°C) at 6-8 h day$^{-1}$ | Standard diets | Fecal samples | *Bacteroidetes* spp. | *Firmicutes* spp. | [84] |
| Broilers | CT (23±1°C) vs HS (34±1°C) for 7 h day$^{-1}$ | Normal protein (NP) diet or Low protein diet fortified with glycine; | caecal | *Clostridia* spp. | *Lactobacilli* spp. | [44] |
| Broilers | HS (30°C) for 24 h+24 h feed withdrawal | Standard diet | Ileal contents | *Salmonella enteritidis* - | - | [15] |
| Broilers | HS at 32°C for 9 h day$^{-1}$ from 15-42 days | Poultry Star (synbiotic supplements consisting *Bifidobacterium animalis*, *Enterococcus faecium*, *Lactobacillus reuteri*, *Pediococcus acidilactici* and *fructooligosaccharide*) | Caecal contents | *Lactobacilli* and *Bifidobacterium* spp. | *Escherichia coli* and *Coliforms*, | [76] |
| Broilers | CT (22°C) vs cyclic HS (33°C for 10 h, at 0800-1800 and 22°C from 1800 to 0800) | Probiotic mixture with *Bacillus licheniformis*, *Bacillus subtilis* and *Lactobacillus plantarum* | Duodenum, ileum and caecal contents | *Coliforms* and *Clostridium* spp. | *Lactobacillus* and *Bifidobacterium* spp. | [16] |
| Shaoxing ducks | CT (25°C), vs cyclic HS (30-40°C) for 15 days | Standard diet | Duodenum, jejunum, and ileum contents | Phylum *Firmicutes*, genus *Lactobacillus* | - | [85] |
| Laying hens | CT (21± 1°C), cyclic vs HS (29-35°C) | Standard diet | Caecal contents | Phyla *Bacteroidetes* and *Firmicutes*; order *Bacteroidales* and *Clostridiales*; genre *Bacteroides* and *Rikenellaceae* | - | [86] |
| Laying hens | CT (26°C ) vs HS (33°C) for 20 days | Probiotic mix containing *Bacillus subtilis* and *Enterococcus faecium* | Ileal and caecal contents | Ileal and caecal *Escherichia coli* increased with HS | *Lactobacilli* in ileal and caecum | [71] |

GIT: Gastrointestinal tract, CT: Control groups, HS: Heat stress groups, vs: Versus strenuous environmental conditions could be drastically reduced using basic designing layouts to enhance poultry production during the hot season. The shape of the pen (semi-open building), ventilation (air movement within and out of the poultry pens to remove ammonia, carbon dioxide and moisture) in hot and moist locations, natural or artificial shading (planting of trees round the pen) and provision of more water for bird consumption[21,22,61] are viable strategies to reduce heat stress. It is also important to consider the type and management of the roofing. The roofs should be clean and rust- and dust free. A rusty or dark-coated roof reflects solar radiation less than those with a shiny surface. Roof reflectivity could be improved by painting and decorating an aluminum roof or with zinc-metallic pigment[61]. Ventilation fans could be used to maintain the temperature in the pens and installing an alarm method that gives signals during ventilation system failure is necessary, especially in the hot season[2]. In addition, reducing the population density of the birds might be important during intensely hot periods[2]. In underdeveloped countries, ice blocks could be provided into the birds' water serving tanks during harsh weather conditions. Environmental conditions must be properly monitored. An environmental modification strategy is a key factor to reduce the effect of heat stress. However, proper management of the environment without a good nutritional program, poultry bird disease management and genetic characteristics cannot alleviate heat stress on poultry farms[2].

**Nutritional management:** Nutritional management such as restricting feed[23,62], adding fat and reducing excess protein[63] have been highly recommended to reduce the adverse impacts of heat stress and enhance the performance in birds[23,62,64]. Lin *et al.*[22] reported that feed restriction (about 60%) for chicks on days 4, 5 and 6 increased growth and the survival rate in response to exposure to heat stress on days 35-41 (marketing age). Kapetamov *et al.*[2] reported that poultry feedstuff should be completely balanced, comprising easily digestible and edible nutrients during severe stressful conditions[2]. Researchers have suggested the use of quality protein and amino acids (e.g. methionine and lysine) to reduce the detrimental effects of high temperature and heat increment[23,62,64]. Diversity and composition in the gut microbiome is highly impacted by varying compositions in poultry diets[13].

**Dietary supplementation:** Nutritional supplements possessing anti-inflammatory and/or antioxidant effects may enhance host immune responses. These effects are achieved via their actions on the microbiota environment, intestinal permeability, liver function and/or immune defenses[65].

Different nutritional approaches were shown to minimally alleviate this effect through the diet by increasing energy composition of the feed, vitamins, minerals and salts antioxidant[66,67] because of a high rate of excretion of vitamins A, C and E and minerals such as selenium, iron, zinc and chromium from the chicken body during hot weather[61,64,66]. Therefore, dietary supplementation of minerals and vitamins and balancing electrolytes could potentially reduce mortality and improve growth in poultry birds in harsh environments[21].

Feed additives and amino acids supplementation were also shown to impact positively on gut health during stress conditions[68,69]. *Lactobacilli* and other bacterial forms within the small intestine compete for amino acids, unavoidably absorbing and using these amino acids for cellular anabolism[70]. L-arginine restored the ileal microbiota composition and functionality of *Clostridium perfringens*-challenged chickens including the *Nitrospira* sp., *Nitrospira bacterium*, *Bradyrhizobium elkanii* and *Pseudomonas veronii*[71]. Amino acids, including threonine, glutamine and arginine may modulate intestinal mucosa functions by improving epithelial turnover rates and, thus, promoting intestinal recovery during an insult[72]. L-arginine was shown to attenuate heat stress-induced intestinal permeability, thereby preserving intestinal epithelial integrity[73].

To enhance the resistance of poultry birds to heat stress, the poultry birds' diet can be supplemented with phytogenic feed additives rich in phenolics and flavonoids[42]. Lan *et al.*[74] also affirmed that the gut microbiota in chickens with a high temperature can be balanced through supplementation of probiotic-based *Lactobacillus* strains, thereby restoring cecal microbial communities during heat stress by shifting the microbiota balance towards equilibrium during stress conditions[74]. During heat stress, supplementation with a probiotic mixture containing *Lactobacillus plantarum*, Bacillus subtilis and *Bacillus licheniformis* improved intestinal *Lactobacillus* and *Bifidobacterium* as well as coliform abundance[16]. The inclusion of probiotics such as beneficial bacteria to improve the gut health status or prebiotics to aid in decreasing the pathogenic bacteria's colonization and enhance competition becomes necessary to maintain the microbiota homeostasis under stress conditions[75]. Additionally, synbiotics, which contain combined advantages for both probiotics and prebiotics, may prove beneficial to improve intestinal nutrient absorption and microbial ecology during heat stress. Mohammed *et al.*[76] showed that broilers fed synbiotics during heat stress had higher bacterial counts of positive microbes, such as *Bifidobacterium* spp. and *Lactobacillus* spp. with a decrease in harmful bacteria counts including *E. coli* and coliforms[76].

The antibiotic growth promoter, Lupulone, induced *Clostridium leptum*, *Clostridium coccoides* and *Bacteroides* in the cecum and the midgut was dominated by *Lactobacillus*, the *Enterobacteriaceae* family and *Enterococcus* whereas *Clostridium perfringens* and *Lactobacillus* were reduced[77]. In addition, osmo-protective supplements might assist in decreasing the recurrence of heat stress, which increases the mortality rate in chickens[9,21].

Furthermore, the application of gut biomarkers such as citrulline[78] in assessing the microbiota status may be functional in evaluating intestinal dysfunction and gut health. Gut health is determined by microbial, nutritional, environmental and host (such as mucosal barrier, immunity) factors[79] and thus, it is necessary to continuously monitor intestinal health status. The use of gut biomarkers to observe changes in the microbiome status would have future health benefits for poultry production. Currently, several genetic strategies including genomic, transcriptomic, proteomic and metabolomic approaches were used to investigate alterations to microbial structures, compositions and functioning. However, future strategies may involve the combinations of several gut biomarkers such as citrulline[80], leptin and ghrelin[81] along with several plasma, urine and fecal biomarkers[82] and/or application of advanced molecular approaches such as metabarcoding and metagenomic, meta-transcriptomic and metaproteomic approaches[79,83].

## CONCLUSION

Gut microbiota in poultry birds are significantly affected when exposed to high ambient temperatures (heat stress). Heat exposure may influence the microbial population, abundance, distribution and functioning within the gut segments. Zoonotic pathogen enrichment and a decrease in beneficial bacteria during heat stress conditions are commonly encountered. Therefore, this study sheds new light on the associations between poultry productivity and gut microbiota function. Understanding the gut microbiota composition during heat stress conditions may provide perspectives on improving poultry growth and performance. Several strategies ranging from genetic to environmental to nutritional factors have been suggested as measures to alleviate heat stress effects on the gut microbiota but detailed investigations are still required to better understand the microstructure of poultry birds' intestinal tract and to explore the role of genetics in microbial functioning.

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