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Board Invited Reviews

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Effects of heat stress on the gut health of poultry

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Abstract

Stress is a biological adaptive response to restore homeostasis, and occurs in every animal production system, due to the multitude of stressors present in every farm. Heat stress is one of the most common environmental challenges to poultry worldwide. It has been extensively demonstrated that heat stress negatively impacts the health, welfare, and productivity of broilers and laying hens. However, basic mechanisms associated with the reported effects of heat stress are still not fully understood. The adaptive response of poultry to a heat stress situation is complex and intricate in nature, and it includes effects on the intestinal tract. This review offers an objective overview of the scientific evidence available on the effects of the heat stress response on different facets of the intestinal tract of poultry, including its physiology, integrity, immunology, and microbiota. Although a lot of knowledge has been generated, many gaps persist. The development of standardized models is crucial to be able to better compare and extrapolate results. By better understanding how the intestinal tract is affected in birds subjected to heat stress conditions, more targeted interventions can be developed and applied.

Key words: gut health, heat stress, poultry, stress

Introduction

Stress is the reaction of the animal organism to stimuli (real or perceived) that disturb its normal physiological status, or in other words, a biological adaptive response to restore homeostasis. However, this definition or concept becomes more complex, when considered that stress can be experienced within a short period of time (i.e., acute stress) and/or during prolonged periods of time (i.e., chronic stress), which can also occur continuously or intermittently. Moreover, it is important to keep in mind that stress is not always negative or detrimental ("distress"), but in some cases, it can actually be positive or beneficial to an individual ("eustress"). Although defining and discussing all the different aspects and types of stress are a fascinating subject, it is out of the scope of this literature review and, therefore, readers are referred to some of the many published studies available in the scientific literature (Selye, 1936, 1955, 1976; Moberg, 1987; Veissier and Boissy, 2007; Koolhaas, 2008; McEwen and Akil, 2020). However, for the purpose of this review, it is critical to understand that the stress response varies between individuals within the same population or observational group, not only because stressors are variable and experienced in different degrees but also because they rarely occur singly. This is particularly important when considering poultry production, where large populations or groups of birds (broilers, layers, turkeys) are kept together and under the same general conditions, but nevertheless, will experience stress in a wide range of magnitude (Stott, 1981; Young et al., 1989; Rostagno, 2009; Koolhaas et al., 2010).

Understanding and controlling environmental conditions are crucial to poultry production, health, and well-being. Heat stress is a top environmental concern in poultry production worldwide, being potentially triggered by a variety of conditions, such as climatic conditions common in some regions of the world, failure of ventilation and temperature controls (manual or automatic systems), inadequate brooding conditions, stocking density at the end of the growing phase, and new or alternative ("open") production systems (e.g., free-range, organic) that create challenges for efficient environmental controls and frequent exposure to the external environment.

Abbreviations

ANS	autonomic nervous system
CNS	central nervous system
ENS	enteric nervous system
HPA	hypothalamus–pituitary axis
HSF	heat shock factors
HSP	heat shock proteins
TJ	tight junctions

Heat stress occurs whenever there is a negative balance between the net amount of heat energy flowing from the animal to the environment and the amount of heat energy produced by the animal (Renaudeau et al., 2012). This imbalance is caused by variations of a combination of several environmental factors (e.g., sunlight, thermal irradiation, and air temperature, humidity, and movement), and characteristics of the animal (e.g., species, metabolism rate, and thermoregulatory mechanisms).

The intestinal tract is particularly responsive to any type of stress, including heat stress (Calefi et al., 2014, 2017; Tellez Jr. et al., 2017; Slawinska et al., 2019). Effective functionality of the intestinal tract is critical to poultry production, as it has major broad implications for the overall health and performance of the birds (Skinner et al., 2010; Kaldhusdal et al., 2016; Kadykalo et al., 2018). However, as a very complex and intricate system, the intestinal tract is still viewed by most as a "black box" with many basic and important gaps of knowledge that still need to be uncovered. Besides, the intestinal tract actively interacts bidirectionally with many other complex systems in the animal's body, such as the neuroendocrine and immune systems, making it very difficult to fully unravel this multifaceted interrelationship. Therefore, this review attempts to provide a concise compilation of the current knowledge and evidence available in the scientific peer-reviewed literature about the impact of heat stress on the intestinal tract of poultry.

How are Stress and the Intestinal Tract Connected?

The brain and digestive systems communicate continuously and bidirectionally through several complex pathways involving the enteric nervous system (**ENS**), the autonomic nervous system (**ANS**), the hypothalamus–pituitary axis (**HPA**), and the central nervous system (**CNS**). This bidirectional network is known as the brain–gut axis. Signals from the brain can modify the motor, sensory, secretory, and immune functions of the intestinal tract, and conversely, visceral messages from the intestinal tract can influence brain functions in a top–down and bottom–up relationship (Bueno, 2000; Bhatia and Tandon, 2005; Jones et al., 2006; Konturek et al., 2011; Brzozowski et al., 2016; Liu and Zhu, 2018; Cryan et al., 2019).

The ENS is an integrative network located within the wall of the entire intestinal tract, containing millions of neurons, and controlling the microcirculation, motility, and all exocrine and endocrine secretions (Goyal and Hirano, 1996; Bueno, 2000; Costa, 2000). Although we are only beginning to understand the complex functionality of the brain–gut interactions involved in stress-related intestinal alterations, there is clear evidence that stress can lead to functional disorders, as well as to inflammation and infections of the intestinal tract. Stress triggers the HPA and the activation of the ANS, as well as an increase in corticosterone levels and proinflammatory cytokines. These downstream signals act via neural connections of the brain–gut axis together with reactive oxygen metabolites, local inflammatory factors, and circulating cytokines, affecting intestinal homeostatic functions (de Kloet et al., 2005; Jones et al., 2006; Lambert, 2009; Ulrich-Lai and Herman, 2009; Konturek et al., 2011; Spiers et al., 2015; Breit et al., 2018; Mukhtar et al., 2018).

Functional intestinal disorders are defined as a variable combination of intestinal symptoms that do not have an identified underlying pathophysiology (Corazziari, 2004). However, besides dysfunction of the gut–brain axis, several other factors play a role in functional intestinal disorders, including low-grade mucosal inflammation and chronic infections, which can be caused by many external factors, such as diet and stress, including heat stress (Spiller, 2004; Holtmann et al., 2017).

Behavioral Effects of Heat Stress

Poultry are endothermic homeotherm animals, which are animals that keep their body temperature within a relatively narrow range over a wide range of environmental conditions by balancing heat production (thermogenesis) and heat loss or dissipation. When birds are subjected to conditions leading to heat stress, behavioral and physiological changes or adaptations occur seeking thermoregulation to restore homeostasis (Yahav et al., 2004; Cangar et al., 2008; Farag and Alagawany, 2018). However, it is very important to keep in mind that in general, although the heat stress response of different types of birds is similar, there are individual variations in intensity and duration within the same population or flock (Mignon-Grasteau et al., 2015; Farag and Alagawany, 2018). This consideration is very important in cases of mild-moderate heat stress conditions in the field, as it poses a challenge for producers to quickly and correctly identify and attempt to correct environmental conditions and minimize negative effects. Another cause of response variation resides in the fact that heat stress is often not experienced in isolation, being usually accompanied by other stressors, such as limited housing space and insufficient ventilation (Rostagno, 2009; Lara and Rostagno, 2013; He et al., 2018; Saeed et al., 2019). Furthermore, there is evidence indicating that much of the variation in response to heat stress is also genetically based (Lu et al., 2007; Soleimani et al., 2011; Felver-Gant et al., 2012; Mack et al., 2013; Mignon-Grasteau et al., 2015; Lan et al., 2016; Monson et al., 2018).

Sensible heat loss does not seem to play an important role in poultry, as limited body surface areas are not covered with feathers (e.g., legs, head, wattle, and comb). Thus, latent heat loss by panting (i.e., increased respiratory rate, consisting of short, quick breathing) is the main mechanism used by poultry for heat dissipation (Marder and Arad, 1989; Tzschentke et al., 1996; Yahav et al., 2004; Mutaf et al., 2009). This mechanism for reducing body temperature is known as respiratory evaporative cooling and is based on heat exchange with the environment through the air sacs (Marder and Arad, 1989; Comito et al., 2007). Air sacs are very useful during panting, as they promote air circulation on surfaces contributing to increase gas exchanges with the air, and consequently, the evaporative loss of heat (Fedde, 1998).

In addition to panting, birds subjected to heat stress conditions will spend less time feeding and more time drinking, as well as more time with their wings elevated, less time moving or walking, and more time inactive (Marsden and Morris, 1987; Lara and Rostagno, 2013; Mack et al., 2013; Bahry et al., 2018). From a practical point of view, under commercial poultry production conditions, it is very important to closely monitor water and feed consumption during periods of higher heat

stress risk. Rapid increase in water and a decrease in feed intake can be good indicators of flocks being subjected to heat stress conditions.

Physiological Effects of Heat Stress

The primary cardiovascular adaptive response of animals under heat stress conditions consists of increasing blood flow to the external surface of the body (i.e., skin) in an attempt to promote heat loss and reduce heat gain from the surrounding environment. However, a compensatory decrease in splanchnic blood flow (i.e., reduced blood flow to internal organs or hypoperfusion) occurs as a mechanism to maintain overall blood pressure stable (Rowell, 1974; Lambert, 2009; van Wijck et al., 2012). The resultant ischemic environment causes a reduced oxygen flow to the intestinal mucosa (i.e., hypoxia), promoting oxidative and nitrosative stress that cause intestinal epithelial tight junctions (**TJ**) to become loose and "leaky." Further damage is caused by the hypoperfusion, due to reduced nutrients and energy to sustain cellular viability and function and, consequently, compromising the turnover of enterocytes occurring along the intestinal tract (Söderholm and Perdue, 2001; Lambert, 2009; van Wijck et al., 2012; Dokladny et al., 2016; Slimen et al., 2016). Also, as previously mentioned, heat stress causes reduction in voluntary feed intake. According to Bernabucci et al. (2009) and Morera et al. (2012), heat stress upregulates the secretion of two adipokines, leptin, and adiponectin, as well as the expression of their receptors. These adipokines negatively regulate feeding behavior, resulting in a markedly reduced feed intake (Richards et al., 2010). This form of caloric restriction allows hyperthermic animals to reduce metabolic heat generation, which otherwise would exacerbate the effects of heat stress (Slimen et al., 2016). However, this abrupt reduction of feed intake leads to additional alterations and damage to the intestinal mucosa, as discussed further ahead.

It is well-known that the exposure to high environmental temperatures results in activation of the HPA and of the brain–gut axis, as well as elevated plasma corticosterone concentrations (Garriga et al., 2006; Star et al., 2008; Quinteiro-Filho et al., 2010, 2012b). In combination with reduced voluntary feed intake, these will affect the functionality of the entire digestive system, leading to changes in motility and flux patterns, secretory activity, content viscosity, and pH (Tur and Rial, 1985; Mitchell and Carlisle, 1992; Geraert et al., 1996a, 1996b; Hai et al., 2000).

It is very important to highlight that nutritional factors, such as diet quantity and composition, markedly affect the regulation of the energy flow in poultry. As already mentioned, exposure to increased environmental temperature leads to reduced feed intake, which in turn leads to reduced maintenance energy requirement, as well as reduced intestinal enzymatic secretory activity (e.g., trypsin, chymotrypsin, amylase). Additionally, the effects described above on the intestinal mucosa compromise digestive functionality, decreasing feed/nutrient digestibility, and increasing feed passage. Moreover, a metabolic shift takes place in birds subjected to heat stress conditions, in which decreased protein and increased lipid deposition occur, as part of the thermoregulatory mechanism, due to the increased energy required to digest protein, in comparison to fat digestion. Therefore, there is a significant reduction of feed efficiency, increased lipid accumulation through increased de novo lipogenesis, reduced lipolysis, and enhanced amino acid catabolism. (Geraert et al., 1996a, 1996b; Bonnet et al., 1997; Hai et al., 2000; Balnave, 2004; Sahin et al., 2009; Slimen et al., 2016; Habashy et al., 2017).

Effect of Heat Stress on Intestinal Integrity

The intestinal barrier is formed essentially by a single layer of enterocytes cells, their membranes, and the TJ between them along the intestinal epithelium, covered by a mucus layer, protected by humoral and cellular components of the local immune system (Vancamelbeke and Vermiere, 2017; Chelakkot et al., 2018). Integrity of the intestinal barrier is of paramount importance in poultry production. Loss of intestinal barrier integrity (or intestinal barrier dysfunction) leads to increased intestinal permeability, which is defined as the non-mediated diffusion of large (i.e., molecular weight >150 Da), normally restricted molecules from the intestinal lumen to the circulatory system (Lambert, 2009). Increased intestinal permeability usually results in harmful local, and possibly systemic inflammatory reactions. This situation is commonly referred to as "leaky gut" (Quigley, 2016; Mu et al., 2017; Chelakkot et al., 2018).

Many different psychological and physiological stressors can negatively impact the intestinal barrier integrity (Söderholm and Perdue, 2001; Hart and Kamm, 2002; Gareau et al., 2008; Lambert, 2009; Keita and Söderholm, 2010). In situations of heat stress, reduced availability of oxygen and nutrients due to the diminished blood supply and reduced feed intake leads to morphologic changes and mucosal damage, resulting from oxidative stress and inflammation. Furthermore, the increased serum levels of corticosterone and catecholamines (epinephrine and norepinephrine) caused by heat stress also affect TJ and the immune system. In fact, several studies (Quinteiro-Filho et al., 2010, 2012a, 2012b, 2017) have demonstrated how heat stress affects the integrity of the intestinal barrier, leading to increased intestinal permeability and local inflammation in poultry, characterized by increased lymphoplasmacytic infiltrate along the small intestine (duodenum, jejunum, and ileum). The presence of heterophils in the observed inflammatory infiltrate reflects bacterial invasion from the intestinal epithelia to the lamina propria. In studies by Quinteiro-Filho et al. (2012a) and Alhenaky et al. (2017), heat-stressed broilers had increased serum concentrations of corticosterone, endotoxin lipopolysaccharide, and systemic inflammatory cytokines, Tumor Necrosis Factor-α and Interleukin-2. In the same studies, higher prevalence of *Salmonella* spp. in spleen and liver were reported (respectively) in heat-stressed birds, as compared with control. The authors concluded that heat stress disrupted the intestinal barrier, resulting in increased intestinal permeability to endotoxin, and translocation of intestinal pathogens. According to the studies by Song et al. (2014) and Wu et al. (2018), the increased intestinal permeability occurring in birds subjected to heat stress are caused by disruption of both, transcellular (intracellular) as well as paracellular (intercellular) TJ disruption.

Interestingly, a study by Varasteh et al. (2015) provided evidence of difference in susceptibility between intestinal segments to heat stress, as demonstrated by the assessment of different biomarkers, including heat shock proteins (**HSP**), heat shock factors (**HSF**), adherens junctions, TJ, cytokines, and oxidative stress markers. Alterations in the level of expression of these biomarkers were more pronounced in the ileum, compared with the jejunum. Upregulated and activated HSFs target the major heat-inducible proteins, such as HSP70 and HSP90, which have a central role in the regulation of protein homeostasis, and are considered as general markers of tissue injury, playing an important role in the protection and repair of cells and tissues (Gu et al., 2012; Arnal and Lallès, 2016). Moreover, the heat stress-induced changes were accompanied by an inflammatory

reaction and tissue/cell damage, likely caused by the intestinal barrier disruption and penetration of pathogens.

Many studies have reported morphometric and histopathological changes occurring in the intestinal tract of poultry subjected to heat stress conditions. The vast majority of these consistently report the observation of reduced villi height and increased crypt depth, leading to lower villi:crypt ratio (Garriga et al., 2006; Burkholder et al., 2008; Bozkurt et al., 2012; Deng et al., 2012; Song et al., 2014; He et al., 2018; Wu et al., 2018). Additionally, Santos et al. (2015) also described the occurrence of increased width of villi base and decreased epithelial cell area, in the duodenal, jejunal, and ileal mucosa in broilers subjected to heat stress.

Effects of Heat Stress on the Immune System

A major component of the immune system is the gut-associated lymphoid tissue, which in poultry consists of lymphoid cells located in the epithelial lining (intraepithelial lymphocytes) and the lamina propria, as well as specialized lymphoid structures, such as Peyer's patches, Meckel's diverticulum, cecal tonsils, and bursa of Fabricius (Lillehoj and Trout, 1996; Bar-Shira et al., 2003; Casteleyn et al., 2010; Nochi et al., 2018). As previously described, the intestinal immune system, CNS, and the endocrine system interact with each other through bidirectional pathways. Moreover, there is plenty of evidence showing that enteric neurons and intestinal immune cells share common regulatory mechanisms and can coordinate their responses to challenges, with various stressors dysregulating the immune response by affecting the interplay of these systems and, consequently, increasing susceptibility to pathogens, influencing the severity of infections and pathologies, and even negatively affecting responses to vaccines (Glaser and Kiecolt-Glaser, 2003; Chrousos, 2009; Shini et al., 2010). It has been shown that lymphocytes, monocytes or macrophages, and granulocytes exhibit receptors for many neuroendocrine products of the HPA and Sympathetic-adrenal-medullary axes, such as corticosterone and catecholamines, which can affect cellular trafficking, proliferation, cytokine secretion, antibody production, and cytolytic activity. This topic has been the subject of several extensive reviews (Ader and Cohen, 1993; Besedovsky and del Rey, 1996; Butts and Sternberg, 2008; Marketon and Glaser, 2008; Ashley and Demas, 2017; Verburg-van Kemenade et al., 2017). However, knowledge continues to be generated, providing increasing insights on the interplay among these systems.

In poultry, the neuroendocrine–immune interaction is no different (Mashaly et al., 1998; Kaiser et al., 2009; Kuenzel and Jurkevich, 2010), and several studies have specifically investigated the effects of heat stress on the immune response. In general, all studies show an immunosuppressing effect of heat stress on broilers and laying hens, based on a variety of measurements, such as reduced number of intraepithelial lymphocytes and Immunoglobulin A-secreting cells along the intestinal tract, reduced antibody response, and reduced phagocytic activity of macrophages (Bartlett and Smith, 2003; Aengwanich, 2008; Niu et al., 2009; Quinteiro-Filho et al., 2010, 2017; Bozkurt et al., 2012, Deng et al., 2012). Lower relative weights of thymus, bursa, spleen, and liver have also been described in broilers and laying hens subjected to heat stress (Niu et al., 2009; Quinteiro-Filho et al., 2010; Shini et al., 2010; Felver-Gant et al., 2012; Ghazi et al., 2012; Calefi et al., 2014; Honda et al., 2015; Aguanta et al., 2018). Moreover, several studies have demonstrated that heat stress can alter the levels of circulating cells, leading to an increase in heterophil:lymphocyte (H:L) ratio, due to reduced numbers of circulating lymphocytes and higher numbers of heterophils caused by the increased circulating concentrations of glucocorticoids, in particular corticosterone, released by activation of the HPA axis (Post et al., 2003; Prieto and Campo, 2010; Shini et al., 2010; Felver-Gant et al., 2012; Honda et al., 2015; Scanes, 2016).

Effect of Heat Stress on the Intestinal Microbiota

The intestinal tract of poultry contains a very complex and highly diversified microbiota, which extensively interacts bidirectionally with the host and utilizes the diet as substrate (Oakley et al., 2014; Shang et al., 2018; Kogut, 2019; Yadav and Jha, 2019). Based on this close and intricate relationship, it is not surprising that the intestinal microbiota is highly susceptible to the effects of a multitude of host and environmental factors, including heat stress. Although it is increasingly recognized that stress modulates the intestinal microbiota community structure and activity, exact mechanisms underlying these effects or responses are still being unraveled (Karl et al., 2018; Kers et al., 2018). In poultry, several studies have shown significant effects of heat stress on the intestinal microbiota composition and structure, both in broilers and in layers. Some specific alterations reported include lower levels of *Lactobacillus* and *Bifidobacterium*, and higher levels of *Clostridium* and total coliforms (Lan et al., 2004; Burkholder et al., 2008; Soliman et al., 2009; Song et al., 2014; Sohail et al., 2015; Kers et al., 2018; Wang et al., 2018; Shi et al., 2019; Zhu et al., 2019). Interestingly, these studies suggest differing effects along the intestinal tract, with the small intestine being more sensitive in comparison to the ceca.

There are several biological pathways through which heat stress can affect directly or indirectly the intestinal microbiota. A lot of this basic research has been done in humans and different animal models. However, the knowledge acquired applies equally to poultry (Lara and Rostagno, 2013; Galley and Bailey, 2014; Scanes, 2016; Karl et al., 2018; Kers et al., 2018). For instance, as previously discussed, reduced feed intake and increased water consumption will affect the availability of nutrients in the intestinal tract to be used as a substrate by the microbiota, as well as trigger a variety of additional changes in the intestinal environment such as patterns of secretory activity and motility, and digesta viscosity (Thompson and Applegate, 2006; Thompson et al., 2008; Lara and Rostagno, 2013; Karl et al., 2018; Kers et al., 2018; Metzler-Zebeli et al., 2019; Xing et al., 2019). Also, the activation of the HPA axis will lead to alterations of the immune system, which in turn will result in altered host:microbiota interactions (Lara and Rostagno, 2013; Galley and Bailey, 2014; Scanes, 2016; Calefi et al., 2017). Moreover, the reduced blood flow directed to the intestinal tract and resulting hypoxia are known to cause marked damage to the mucosa, leading to the occurrence of oxidative stress and inflammation, and consequent disruption of the intestinal integrity (Lambert, 2009; Galley and Bailey, 2014; Scanes, 2016; Karl et al., 2018). With the intestinal barrier compromised, bacteria present in the intestinal lumen gain access to the host, potentially becoming systemic.

Although the impacts of many different factors, including stress, on the intestinal microbiota have been an area of great focus recently, there is still a major need to better and more specifically understand the consistency of the reported effects, as

well as the consequences. It is very easy to detect discrepancies or divergences between studies on the reported results, probably due to the complexity of the intestinal microbial ecosystem, and the number of confounders included. More standardized models and methodologies are needed to better unravel the response of the intestinal microbiota to stressors in general, and heat stress specifically, in poultry.

Heat Stress as a Food Safety Risk?

Environmental stress is known to be a factor that can lead to increased colonization of animals by pathogens, fecal shedding, and horizontal transmission (Humphrey, 2006; Rostagno, 2009; Verbrugghe et al., 2012; Alverdy and Luo, 2017). As previously discussed, stress-induced loss of intestinal barrier integrity, disruption of immune response, and perturbation of the intestinal microbiota compromise innate protective mechanisms and increase the potential for pathogens, such as *Salmonella*, *Campylobacter*, and *Escherichia coli*, to colonize the intestinal tract and invade the host. Such colonization in poultry will increase the risk of carcass contamination during processing and will increase the potential for *Salmonella* to translocate to the reproductive tract, where it can contaminate eggs and chicks during formation. For instance, using an ex vivo approach, Burkholder et al. (2008) showed that mucosal attachment of *Salmonella* Enteritidis increased when tissues originated from heat-stressed birds. Also, according to Quinteiro-Filho et al. (2010, 2012a), increased inflammation and translocation of *Salmonella* Enteritidis were observed in broilers subjected to heat stress, resulting in increased levels of the pathogen in spleen samples. In another study, heat stress in broilers also increased *Salmonella* colonization in the crop and cecum, as well as an invasion to the spleen, liver, and bone marrow (Quinteiro-Filho et al., 2017). In fact, several epidemiological studies have reported seasonal effects on the occurrence of *Salmonella* and *Campylobacter* in flocks of broilers and laying hens, as well as in retail poultry products (van der Fels-Klerx et al., 2008; Jorgensen et al., 2011; Sibanda et al., 2018; Velasquez et al., 2018; Smith et al., 2019).

Therefore, it is reasonable to speculate that a direct consequence of the heat stress effects described in this review would lead to increased contamination risk of animal products and consequent increased food safety risk. Understanding the mechanisms by which heat stress alters normal intestinal characteristics and induces susceptibility to colonization and infection is an important first step in designing on-farm strategies aimed at reducing pathogen contamination in poultry.

Conclusions

As described in this review, the intestinal tract is very sensitive and responsive to heat stress and a variety of changes can be observed, including physiological and immunological responses, as well as impairment of the intestinal integrity and inflammation, and marked alterations in the microbiota. However, there is a lot of variability in the magnitude of these effects, essentially due to the complex multifactorial nature of heat stress, and broad variation on how birds within a group or population experience and react/adapt to such conditions.

As we strived to present a concise overview of the topic, many gaps of knowledge were encountered, such as differences between acute (which could occur singly or multiple times during periods of time) and chronic heat stress, age differences, and possible early-life experience leading to adaptation, nutrition, and feeding approaches to manipulate diet thermogenesis, and how changes in production systems affect risk and response to heat stress conditions. However, as every coin has two sides, we should look at this as an incredible open field of opportunities for talented and curious scientists to explore.

Worth mentioning is that intervention strategies to deal with heat stress conditions have been the focus of the vast majority of published studies, applying different approaches, mostly focusing on nutritional manipulation (i.e., diet formulation according to the metabolic condition of the birds), as well as the inclusion of feed additives in the diet (e.g., antioxidants, vitamins, minerals, probiotics, prebiotics, phytogenics) and water supplementation with electrolytes. Nevertheless, effectiveness of most of the interventions has been variable or inconsistent, likely due to variable study conditions and many confounders. There is a clear need to establish some basic common parameters and models to allow for better comparison and extrapolation of reported results from different studies, particularly if they are to be applied in commercial settings.

Heat stress is one of the most important environmental stressors challenging poultry production worldwide, leading to reduced production performance and decreased poultry and egg quality. However, a major concern should be the negative impact of heat stress on poultry welfare, which is clearly not sufficiently addressed in the scientific literature, as it should. The same is true for commercial production systems, where birds may still maintain relatively satisfactory productive performance, but at a negative individual's well-being cost. Obviously, plenty of room exists for improvements in understanding and dealing with heat stress in poultry production.

Conflict of interest statement

The authors declare no real or perceived conflicts of interest.

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