



Turkeys



Ducks



Layers



Broilers

Webinar Abstract

Effects of Heat Stress on Monogastrics and Micronutrient Supplementation

The aim of this Webinar is to elucidate how heat stress affects monogastric system biology and how does this in turn translate in performance losses. An assessment of production losses along with their aetiology in relation to monogastric species at different stages of production is provided (broilers, growing finishing pigs, laying hens and sows). Finally, an overview of certain micronutrients which are regularly included in premixes, or provided in heat stress conditions, for which there is an extensive body of literature is presented in relation to their importance and levels of supplementation.

Part I. Heat Stress Effects on Productivity

Heat stress (HS) effects (exposure to temperatures above the thermoneutral zone-upper critical temperature threshold) in livestock animals depend on the nature of the heat stress event (defined as external heat load) and to internal heat load which relates to the characteristics of the breed/animal /physiological stage and its metabolic heat production. Animal production processes are exothermic in nature. When faced with heat stressed animals, repartition nutrient resources away from growth towards heat dissipation functions (respiration-evaporative losses). In an attempt to reduce internal heat load, animals firstly reduce their feed intake, which mainly explains losses in productivity. Feed intake reduction is related to altered neuropeptide signalling and reduced blood flow to the intestinal tract, which moves towards the skin to facilitate heat dissipation, and is related to altered gut motility and function.

Part of the metabolic inefficiency ascribed to heat stress is related to mitochondrial damage and the associated oxidative stress. The disturbed mitochondrial electron flow leads to increased production of Reactive Oxygen Species (ROS) and induction of nitrosative stress. Peroxidized products of lipid and protein metabolism (lipid peroxides and protein carbonyls) are accumulated, which damage cells particularly in tissues with high mitochondrial potential and high energetic demands and protein synthesis potential (such as breast muscle in broilers). In turn oxidative stress is linked with the activation of transcription factor NFκ-B and an inflammatory cascade is initiated, which alters metabolism and leads to metabolic inefficiency.

The gastrointestinal tract and enterocytes in particular are highly sensitive to oxidative stress associated to heat stress due to the hypoxic conditions linked to the reduced blood flow. Gut barrier function is challenged with the expression of several classes of tight junction proteins being reduced. Increased gut permeability in both pigs and poultry leads to local injury and inflammation, which becomes systemic by the increased passage of luminal endotoxins. Reduced digestive enzyme secretion and gross morphometric and histopathological changes, typically occur. As a result, nutrient digestion and absorption is adversely affected.

As far as metabolism is concerned, heat stress and inflammation share many common features such as reduced thyroid production, increased glucocorticoid production, insulin resistance and disrupted endocrine function. These metabolic/hormonal alterations essentially reduce the animal's heat load as anabolic functions are thermogenic in nature and especially protein synthesis. At the same time, they support the animal's altered metabolic requirements in order to support the increased requirements of the activated immune system. Collectively, these changes lead to increased proteolysis and reduced protein synthesis, which are essentially the processes governing the synthesis of meat, egg, milk and foetus development. On the other hand, fatty acid synthesis is enhanced, and lipolysis is hindered. These events lead to fatter carcasses but also to a reduced capacity for the lactating sow to utilize the body reserves for milk synthesis.

Part II. Effects per Species

Effects of heat stress are not limited to animal performance. Oxidative stress and altered metabolism lead to the production of meat and eggs of inferior quality. Overall, increased fat deposition and meat with altered water holding capacity, pH and increased cook and drip losses along with a higher incidence of Pale Soft Exudative meat (PSE) are observed. Eggs have typically reduced mass, shell strength, Haugh units and reduced oxidative stability and pigmentation.

It is important to take into account that modern high producing genotypes, across species and productive stages, are thought to be less resistant to HS; increased genetic selection for production traits (i.e., lean tissue accretion, milk yield, and fecundity) leads to reduced HS tolerance as these processes are associated with increased metabolic heat production. Because of continuous genetic selection for performance traits problems imposed by HS are expected to further aggravate the problem of farm animal susceptibility to HS.

Across all species the magnitude of responses to heat stress are related to the characteristics of heat stress (whether it is cyclic, how long does it last, the age at which it occurs etc.). For broilers heat stress is age dependent, birds being more sensitive at increasing age and is usually of relevance after 3 weeks of age. Losses attributed to reduced feed efficiency, beyond reduction in feed intake, are more prevalent with increasing heat stress intensity or duration. In broilers an increased incidence of footpad dermatitis due to increased water excretion may occur, depending on housing conditions and macronutrient formulation criteria, while lameness due to reduced activity levels occur. There is an obvious and pronounced increase in mortality rates.

In growing finishing pigs, thermotolerance is weight dependent; the higher the body weight the more sensitive they are due to increased backfat thickness (therefore reduced efficiency to dissipate heat) and due to a decreased surface area-to mass ratio. Therefore, effects of heat stress are more pronounced during the finishing phase. On the short term, heat waves may even reduce pig body weight, while in the long-term exposure to hot conditions reduce weight gains and delay the days to slaughter and may affect feed efficiency.

Layers are particularly vulnerable to heat stress because they have to maintain a long production cycle (50 to more than 80 weeks) and heat stress has been shown to affect egg production rate, egg quality and lead to increased mortality. Beyond a reduction in Feed intake and oxidative stress, these events are underlined by endocrine dysregulation, which leads to ovarian dysfunction along with a reduced blood flow to the uterus. Due to the respiratory alkalosis, there is a decrease in blood ionic Ca and blood chemistry, which direct impairs shell mineralization and consequently egg quality.

Sow are affected by heat stress during early gestation similarly due to endocrine dysregulation/Ovarian dysfunction showing reduced fertilization and embryo implantation. During late gestation the reduced uterine

blood flow impairs foetus development. Collectively these events lead to reduced conception rates, number of piglets born and of those born alive. During lactation a combination of reduced feed intake, mammary blood flow and the altered metabolic efficiency (blunted lipolytic response) lead to an inability to meet milk production potential and therefore affect piglet growth).

Part III. Micronutrient Requirements

This part concerns mineral supplementation levels related to i) Na and K and their constituent electrolytes, ii) Micro-minerals which act as co-factors to the endogenous anti-oxidant system, iii) vitamins which participate in detoxification reactions (A, C, E). Betaine is also covered as it relates to glutathione production (GSH) and has been extensively studied. iv) Plant secondary metabolites, which may up-regulate the endogenous anti-oxidant system and negate the adverse effects of inflammation.

1) The events that undermine the acid-base balance disruption are initiated by increased panting to dissipate heat, which results in increased clearance of blood CO₂ that increases blood pH, leading to alkalosis. To counteract alkalosis the kidney increases bicarbonate excretion (HCO₃⁻) which is depleted along with Na⁺ and K⁺ which are increasingly excreted via the urine and feces. For this reason, primary importance to increase alkalogenic minerals K⁺ and mostly Na⁺ whilst maintaining the Cl⁻ to protect the electrolyte ratio and offer a source of HCO₃⁻. The general recommendation for broilers is to formulate with a higher DEB (electrolyte balance, MEq 250), while the preferred electrolyte is NaHCO₃, both in water and feed, which allow to balance the electrolytes level in blood. Higher level of Na in water leads to increased water intake and consequently feed intake. Also, Na increase feed appetite and can enhance feed consumption. In hens NaHCO₃, replenishes depleted HCO₃⁻ and may ameliorate eggshell mineralization. Pigs and sows are less researched but common mechanisms are shared amongst species.

2) As the first response to increased ROS production results there is an initial activation of endogenous anti-oxidant systems Nrf-2 (SOD, CAT, GSH-Px, HO-1) which are depleted with time. Zn and Se are co-factors to endogenous enzymes, which directly neutralize oxidants (Cu/Zn- SOD Se-GSH-Px). Zinc has several biological functions and practical rations are limited in inclusion levels by EFSA (150mg/kg for piglets, sows, 120mg/kg for poultry). Organic forms are often more bioavailable than inorganic forms. In heat stress conditions, a higher supplementation level may be implemented although there is a wide variation in the literature to what is considered the optimum range for beneficial effects on performance (30-100 mg/kg) under heat stress condition, depending on trial specifics. Overall, a minimum supply of 50mg/kg as the bare minimum is required considering its multiple roles, beyond heat stress. In pigs, positive effects on intestinal barrier function and immune function have been observed although evidence for increased performance is lacking. Se has to be supplied via the premix and organic forms are more bioavailable, although this comes at a cost. Multiple studies in poultry have been carried out in heat stress conditions showing that Se supplementation at a range of 0.2-0.5 mg/kg improves performance of layers whilst in broilers most studies show positive effects. In growing pigs and sows supranutritional levels (> 1 mg/kg, confounding with legislation) have shown some positive effects on gut health and preweaning survival, respectively. Nonetheless, dose response studies are needed and more evidence in support of improved performance.

3) The second level includes the detoxification and regeneration reactions of the small molecule antioxidants working at the same time with the first level: vitamins A, E, C and glutathione. Betaine, although not exactly a micro-nutrient in that sense, has attracted a lot of attention in heat stress conditions mainly due to its osmoprotectant

effects and to its methyl donor activities (synthesis of glutathione and replenishing methionine). Addition on top with 500-2000 mg/kg has been shown efficient in laying hens and the majority of studies in broilers show improved performance. In both gestating and lactating sows studies show improved reproduction outcomes (>2200 mg/kg). In finishing pigs published results do not indicate benefits from its supplementation. More recent studies show that macronutrient formulation factors and inclusion of other methyl-donors may reduce obtained benefits from its supplementation, but further research is required. It has been argued that vitamin C synthesis in poultry may be inadequate and it functions as a water-soluble antioxidant. Supplementation may yield positive effects in poultry but its stability during the feed manufacture process and its price are limiting factors. Studies from its addition to water are conflicting reporting both positive effects, and no effect. Vitamin E is a very important lipid soluble antioxidant and studies have looked at supranutritional supplementation levels, levels way beyond what is considered as the requirement according to nutrient recommendations. In finishing pigs 200mg/kg have been shown to have limited effects whilst in poultry levels between 150-500 mg/kg have shown positive effects. Overall, premixes should contain higher quantities than usual, but one has to bear in mind that boosting the anti-oxidant system with other micronutrients, as previously described or when using plant extracts, may reduce actual requirements. During the presentation, several other micronutrients are briefly presented, which are a subject of scrupulous research at CCPA in terms of their optimal supplementation level.

4) Several plant extracts (or in fact their constituent plant secondary metabolites) have remarkable activities in heat stress conditions. Their activities are related to an upregulation of the endogenous antioxidant system (Nrf-2), therefore neutralizing oxidative stress when it occurs while downregulating inflammation by blocking transcription factor NFκ-B. Furthermore, there are other biologically relevant activities, which are a subject of research by CCPA. The most established ones in cases of heat stress are curcumin (turmeric extract), resveratrol (grapes) and epigallocatechin gallate (EGCG-tea extract), which share some favorable characteristics. They have increased bioavailability; although they act on gastrointestinal tract, they are also distributed to other target tissues. A large body of evidence exists in poultry illustrating their beneficial effects exists. Although the research done in pigs is lacking they are increasingly investigated with positive effects observed. There are other plant extracts, which may yield beneficial effects but more research is required. In CCPA, research projects are carried out to assess the most relevant biological activities in cell cultures as well as animal studies within our research facilities and in collaboration with external partners (Brazil, India, Greece). The aim of these studies is to identify the most effective solutions, taking into account their potential synergisms (when using the right combinations and doses). A separate case can be done for capsaicin, which acts on facilitating heat dissipation initially via its actions on TRVP-1 receptor, which is active in pigs. Subsequently, it stimulates intestinal blood flow increasing intestinal absorptive counteracting the effects of heat stress on intestinal blood flow. On the long term, it increases thermotolerance by setting the upper critical temperature higher, meaning that pigs do not feel as hot as they usually do.

Overall, the approach of CCPA is to critically 1) evaluate micro-nutrient supplementation levels, which ameliorate heat stress in an economic viable context, 2) research plant secondary metabolites metabolite activities and test them to identify the best combinations and doses offered, 3) identify the ideal macronutrient formulation in a heat stress context. These axis lead to our products Delta® ThermoPoultry, Thermo® Control, and FeedStim®. In the presentation, some outcomes from our studies, which test our solutions, are presented.