REVIEW ARTICLE | 85

Impaired Reproductive Performance of Dairy Cows under Heat Stress

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Summary

Hot seasons of the year are accompanied by significant losses for dairy farmers. Stress in cattle breeding causes various physiological disorders of vital organs and systems, including nervous, cardiovascular, and endocrine pathologies. Heat Stress (HS) affects the reproductive performance of cows at various physiological stages (pregnancy, calving, the postpartum period) and that manifests in fertility decrease and even leads to culling. Understanding the mechanisms and effects of high temperatures on the reproductive function of productive animals will allow minimizing the impact of HS by implementing appropriate heat-reduction strategies, adjusting nutrition, and breeding heat-tolerant cattle. Thus, a well-considered and timely implemented HS control strategy will prevent reproductive losses and reduce economic losses in the dairy industry.

Key words

dairy cows, reproductive performance, heat stress

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Introduction

Due to the recent climate changes, heat stress is becoming a global phenomenon relevant not only for countries with hot climates but also for those with temperate climates (Solymosi et al., 2010; Dunn et al., 2014; Schüller, 2015; Vaculikova and Chladek, 2017; Herbut and Angrecka, 2018). The economic losses caused by Heat Stress (HS) are huge and amount to billions of dollars even in the developed countries that can afford to implement effective mitigation strategies (Bagath et al., 2019; Becker et al., 2020; Tao et al., 2020 Wankar et al., 2021).

Recent studies suggest that one of the most common and significant stressors is heat, as it has extremely negative effects not only on the health and productivity of dairy cattle but also on the reproductive performance of animals (Habeeb et al., 2018; Sammad et al., 2020; Chen et al., 2021).

Stress is provoked by the damage of the nervous and endocrine systems at different levels of their organization due to the changes in regulation that occur as reflexes in response to strong pathogenic stimuli (Gajdej, 2012). Such stimuli can be climatic factors, individual management decisions (housing type, housing density, number of animals, indoor climate, nutrition and water quality), veterinary and zootechnical measures related to vaccination, animal sanitation, weighing, castration, etc. (Grabovs'kyj, 2012; Azhmuldinov et al., 2018; Narayan et al., 2021). Stress has already become one of the most serious problems in animal husbandry as it occurs much more often than individual diseases of infectious and non-infectious etiology (Grabovs'kyj, 2012; Etim et al., 2014; Kurdeko and Bogomol'ceva, 2017).

HS should be considered in terms of the general adaptation syndrome of stress in animals and some specific features of HS according to the recent studies on this issue. The underlying reason of the stress is the inability of animals to adapt to changes in environmental conditions and intensive technologies of animal husbandry due to the mismatch between the biological nature of the organism (its physiological capabilities) and the environment (Dantzer and Mormède, 1983; Pljashenko and Sidorov, 1987; Tunikovs'ka, 2020; Fatjó et al., 2021). Numerous studies indicate that heat stress is the cause of various disorders in the functioning of vital organs and systems resulting in a chain of adaptive and protective reactions that change nervous, hormonal, and metabolic processes (Agarwal et al., 2012; Gajdej, 2012; Yaribeygi et al.,2017).

Due to this, a deeper study of the causes and the development of HS is necessary. It is important to look for the methods of early diagnosis of HS and the ways of reducing its damaging effects on the reproductive function of productive animals. This is the purpose of this literature review.

The Effect of Heat Stress on the Physiology of Dairy Cows

The optimum temperature (thermoneutral zone) for a dairy cow is within the range from 4 °C to 16 °C. Temperature increase above 22 °C makes it difficult for heat to be released from the body surface of animals by evaporation. The higher the temperature in the barn, the less heat the cow can give off to the environment. If the temperature exceeds the permissible limits of

the thermal neutral zone, the animal develops HS accompanied by physical deterioration and reduced productivity, adversely affecting feed intake, immunity and reproductive performance. Prolonged exposure of animals to high temperatures, especially when combined with high humidity, can lead to heat stroke and even death (West, 2003; Kadokawa et al., 2012; Pasjechko and Nezhlukchenko, 2018; Koshshavka et al., 2019).

All the conditions described can be more severe and cause more complications in highly productive animals. These animals are more susceptible to HS because they have higher metabolic activity than low-yield cows. Thus, in high-performing dairy cows stress occurs at temperatures above +25 °C and even sometimes +20 °C (Kennedy, 1999; St-Pierre et al., 2003; West, 2003; Vaculikova and Chladek, 2017; Kapshuk, 2020).

Overheating influences cows' behavior, their physiological processes, energy homeostasis and the antioxidant system, resulting in deterioration of the general condition and reproductive performance. It results in reduced milk yield, and milk quality (lower fat and protein content), increased risk of mastitis, endometritis, etc. (Koshhavka et al., 2018; Liu et al., 2019; Sklyarov et al., 2020).

The situation is complicated by the fact that during intensive operation on large dairy complexes, cows are actually under constant stress (Wheelock et al., 2010; Atrian and Shahryar, 2012). They need to eat a lot of feed, digest it quickly and constantly pump a lot of blood through the udder because that's the only way they can produce milk. That is, a high-yielding cow can be compared to a marathon athlete. But not every cow is capable of this, just as not every human can run marathon distances (Kekana et al., 2018; Tao et al., 2020; Li et al., 2021).

Stress reactions to nonspecific systemic actions lead to changes in molecular mechanisms in the body that disrupt regulatory reactions, functional and structural homeostasis in stressed cells and tissues (Raza et al., 2021).

The natural body response to HS is the reduction of metabolism by changing the levels of some hormones in the blood. Thus, the levels of growth hormone, triiodothyronine, and thyroxine are decreased, whereas the levels of adrenaline and noradrenaline are increased. That reduces the rate of food passage through the digestive tract and limits food intake. A 10-fold increase of cortisol inhibits the release of oxytocin reducing milk production and increasing the amount of residual milk during milking. On average, up to 10-17 percent of high-fat milk remains in the udder which can provoke mastitis. In addition, cortisone reduces the synthesis of milk protein in udder cells, disrupts the estrous cycle, delays ovulation, suppresses immunity (Aggarwal and Upadhyay, 2013).

HS is accompanied by oxidative stress. Animals usually have mechanisms that protect them from the development of oxidative processes (superoxide dismutase, catalase, glutathione peroxidase). However, these protective mechanisms are limited because stress significantly increases the need for vitamins (ascorbic acid, tocopherols, carotenoids) and microelements (Se, Cu, Zn) (Farooq et al., 2010; Pragna et al., 2017; Kamal et al.,

Numerous studies show that the activation of lipid peroxidation processes triggers cell damage in animals (Beljavskij et al., 2004). Researchers (Vinogradov, 2007; Gudz 'and Beljavskij, 2015; Bagath et al., 2019; Dahl et al., 2020) confirm that the processes of free radical oxidation and rearrangement of the neuroendocrine regulatory link with the subsequent development of immunodeficiency play a major role in stress. In their studies, Herbut et al. (2018) indicate that the signs of the negative impact of HS often appear not at once but later due to the delayed effect (when the negative effects of summer HS can occur in the fall).

Heat Stress and Reproductive Performance of Dairy **Cows (Stress-Induced Infertility)**

Stress is extremely disruptive for all the physiological functions, it is especially harmful to the reproductive system that is one of the most sensitive (Tatarchuk, 2006; L'ovkina, 2016; Seliukova et al., 2019).

The issue of HS is complicated because even one-time exposure to HS results in negative processes that can last up to six weeks (Kamal et al., 2018). HS is always accompanied by oxidative stress, and therefore the body's need for antioxidants to combat oxidizing agents increases significantly (Mylostyva et al., 2022). The immune system is depressed because the destroyed cellular membranes are the gateway to infectious diseases. Changes in the hormonal status affect the reproductive performance of animals. Reproductive diseases become more frequent, and fertility can decrease by 40-50 percent (St-Pierre et al., 2003; Pragna et al., 2017; Zhelavskyi et al., 2021).

Decreased fertility has been associated with the detrimental effects of HS on oocyte maturation and early embryo development (Jordan, 2003; Dash et al., 2016). Numerous reproductive processes are impaired, including oocyte competence, embryo growth, gonadotropin secretion, ovarian steroidogenesis, corpus luteum development, and uterine endometrial function (Badinga et al., 1993; Hansen, 2009; De Rensis et al., 2015; Wolfenson and Roth, 2019).

López-Gatius and Hunter (2020) indicate that previously identified changes are related to changes in local ovarian temperature because ovarian follicles and oocytes are the most sensitive to hyperthermia. The effects of elevated temperatures are associated with increased production of reactive oxygen species that induce cellular apoptosis and disrupt the development of fertilized oocytes. In addition, reproductive disorders during HS are associated with changes in progesterone levels and a decrease in estradiol production in ovarian follicles (Wolfenson et al., 1995, 1997; Khan et al., 2020).

Because of the disrupted gonadotropin secretion follicle development is disrupted, steroid production and plasma progesterone concentration are reduced. Such changes are associated with impaired estrus, decreased oocyte development and embryo survival, as well as pre-implantation (Roth, 2020).

HS reduces the effect of the dominant follicle which is associated with a decrease in the steroidogenic capacity of its folders and granulosa cells and a decrease in the concentration of estradiol in the blood. Plasma progesterone levels may be increased or decreased depending on whether the HS is acute or chronic and on the metabolic status of the animal. These endocrine changes reduce follicular activity and alter the mechanism of ovulation leading to a decline in the quality of oocytes and embryos. The uterine environment changes, which reduces the likelihood of embryo implantation. The negative influence of HS on reproduction is associated with changes in the hypothalamus, pituitary gland, or gonads. However, it is believed that the main effect of HS occurs in the brain or pituitary gland (Khodaei-Motlagh et al. 2011).

Changes in behavior according to HS are associated with less intensive estrus, decreased fertility, impaired physiological course of pregnancy, calving, and the postpartum period (Avendaño-Reyes et al., 2010; Takahashi, 2012; Dash et al., 2016).

Studies show that the probability of successful fertilization in the hot months of the year can drop to 10 percent compared to 40-50 percent at the optimum temperature (De Rensis and Scaramuzzi, 2003; et al., 2015). Krishnan et al. (2017). It was found that with the temperature-humidity index (THI) of over 70, the increase of THI by one unit resulted in a 4.6 percent decrease in the conception rate. HS during pregnancy slowed down fetal growth and led to lower calving weights in newborns. However, it is not easy to quantify the reduction of fertility due to HS as its effects can be both immediate and long-lasting (Negrón-Pérez et al., 2019).

The main effect of HS on reproduction is the delay in the restoration of full estrous cycles in cows after calving; cows tend to come into heat less frequently, and the heat periods are incomplete. This complicates timely detection of optimal insemination time and reduces the likelihood of fertilization (Hansen, 2004; Allen et al., 2015; Collier et al., 2017). As a result, it leads to an increase in the number of service periods and an increase in the number of cows culled due to loss of reproductive performance (St-Pierre et al., 2003).

According to the authors (Huber et al., 2020), impaired fertility in cows due to HS is caused by molecular changes in the glucocorticoid response of the ovaries caused by epigenetic modifications during fetal development. In response to stress, the adrenocorticotropic hormone stimulates the synthesis and secretion of glucocorticoids which can have a detrimental effect on the hypothalamic-pituitary-gonadal axis and estrous cyclicity.

In pregnant cows, HS that is caused by high ambient temperatures leads to modifications in epigenetics of embryo development; this can lead to further phenotypic changes in the adult animal and even affect its offspring (Huber et al., 2020).

Tao and Dahl (2013) determined that HS at the end of gestation affected the development of the placenta which led to hypoxia of the fetus and growth retardation, including the postpartum period. This may have a residual effect on a cow's reproductive system after calving (Lewis et al., 1984).

HS negatively affects the dry period of cows. As a result, milk production during subsequent lactation in high-yielding cows can be reduced by 450-900 kg. In addition, the growth of the fetus is slowed down because less blood enters the uterus, and therefore, there are not enough nutrients for the normal development of the fetus (Table 1). (Guo et al., 2016).

Table 1. The possible effects of heat stress on dairy cows' reproduction

| Targets | The nature of the damage | Authors |
|-----------------------------|--|---|
| Reproductive tract of a cow | Disorders of oocyte competence, corpus luteum development, and uterine endometrial function | Hansen, 2009; De Rensis et al., 2015; Wolfenson and Roth, 2019 |
| Endocrine system | Change in progesterone levels and decreased estradiol production by ovarian follicles. Disorders of gonadotropin secretion. Decrease in the concentration of estradiol in the blood. | Wolfenson et al., 1995, 1997; Khodaei-Motlagh et al. 2011; Roth, 2020 |
| Estrous cycle | Endocrine changes in the organism. Delay in the recovery of full-fledged estrous cycles in cows after calving. | Hansen, 2004; Collier et al., 2017; Khan et al., 2020 |
| Fetus | Uteroplacental vascular insufficiency. Fetal hypoxia. Retardation of fetal growth. | Guo et al., 2016; Negrón-Pérez et al., 2019 |
| The immune system | Depression of the immune system. Spread of diseases and disorders of the reproductive system | St-Pierre et al., 2003; Pragna et al., 2017; Dahl et al., 2020 |
| Organ and tissue cells | Increased reactive oxygen species and lipid peroxidation products. Development of oxidative stress | Sklyarov et al., 2020; Mylostyva et al., 2022 |
| Genes | The genetic modifications of the development of the embryo; phenotypic changes in the adult animal and offspring. | Huber et al., 2020 |

Although HS directly affects reproduction, its effects depend on the intensity and duration of exposure to high temperatures, the amount of milk yield, the stage of lactation, breed, the composition of the diet, level of dry matter intake and physical activity of animals. Samal (2013) believes that to control HS we need further research. We need to better understand the relationship between climatic conditions and reproductive physiology and to assess the effectiveness of different feed, environmental and reproductive strategies in a given region.

Prevention of Heat Stress Effects on the Reproductive Performance of Dairy Cows

Reproductive reactions to HS in dairy cattle are undoubtedly complex, and a single solution to this problem does not seem possible. In dairy farming, the main strategies for minimizing the effects of HS (Krishnan et al., 2017; Negrón-Pérez et al., 2019) are modification of the environment, feeding management, and breeding thermotolerant cattle.

In places where it is impossible to maintain a comfortable maintenance environment for cattle, HS reduction technologies are used (West, 2003; Atrian and Shahryar, 2012; Ahmed et al., 2015). The simplest method to minimize HS in cows is to provide them with sufficient clean water (Bjejer, 2018). It has proven to be effective for cooling cows and for improving feed intake (Mader and Davis, 2004). Therefore, animals need constant access to fresh, clean and cool water. Water needs double at a temperature of about 27 °C if compared to 5 °C. Thus, the animal will drink 170 liters or more instead of 110-115 liters of water per day.

Optimal housing conditions must be provided for animals. First of all, it is effective ventilation of the premises, free access to clean water, more frequent feeding and shifting time of feeding to cool hours of the day (Davis et al., 2003). It is also necessary to make changes in the nutritional value of feed and introduce special feed additives such as buffers, probiotics, a complex of biologically active substances (Otchenashko, 2014). More and more agents in the form of antioxidant drugs are available for the treatment of the HS effects (Boni, 2019).

Modification of animal feed can also improve the immune response of dairy cows to HS. Thus, according to Bagath et al. (2019) supplements with minerals, vitamins, antioxidants, and yeast can improve the immune status of animals. According to Soltan (2010), chromium supplements have shown a tendency to improve reproductive performance, as indicated by an increased percentage of pregnant cows. Therefore, the use of dietary chromium can be considered as a management technique for reducing the effect of HS in dairy cattle. Aréchiga et al. (1998) indicate that additional β -carotene in the diet of animals may increase the fertility rate of cows in summer.

Cooling is the predominant strategy of mitigation of the HS effects. It involves indirect cooling through modification of the environment in the animal's room by ventilation (with or without water) or direct evaporative cooling from the surface of the cow's body by a combination of wetting and ventilation. Currently, the most efficient are the systems that combine evaporative cooling with a tunnel or cross ventilation (Kadokawa et al., 2012; Roth, 2020).

The results of experimental studies by Bucklin et al. (1991) and Akbar et al. (2021) show that those cooling systems (sprinkler and fan cooling) together with shade and grazing at night are the environmental modifications that can improve the comfort of cows and increase milk production in cows in hot, humid climates.

Long-term and short-term strategies of mitigation of HS effects on fertility as well as monitoring of feeding and housing conditions should include measures of mastitis reduction, the use of artificial insemination more often, allied hormonal intervention, and the use of embryo transfer technology (Roth, 2020; Sammad et al., 2020). Thus, Baruselli et al. (2020) believe that genetic selection of donors according to effective thermoregulation ability is one of the potential strategies for mitigating the effects of HS and increasing embryo production in the warmer months.

In addition, the use of embryo transplantation protocols that do not require the detection of estrus in recipients has facilitated management and improved the effectiveness of embryo transplantation programs during HS. Such alternatives allow embryos to be transferred more efficiently during HS periods, by controlling the timing of ovulation (Pereira et al., 2013; De Rensis et al., 2015; Dirandeh et al., 2015; Negrón-Pérez et al., 2019).

The use of an effective cooling system to maintain normothermia in cows is a prerequisite for any additional approach to recovery (Wolfenson and Roth, 2019); the recipient cows' body temperature is crucial during embryo transfer; hormonal procedures that support corpus luteum function and embryo survival are more effective at normal body temperature.

Given that the effect of HS on fertility is multifactorial, a combination of treatments may be the most effective. In particular, combinations of GnRH and PGF 2a are used to improve fertility, and embryo transfer and progesterone use also improve cows' fertility (Wolfenson and Roth, 2019).

De Rensis et al. (2015) propose a hormonal strategy that involves the use of combinations of GnRH, eCG, and hCG in progesterone-based synchronization protocols to increase fertility by artificial insemination, the use of progesterone in the late embryonic and/or early fetal period to reduce pregnancy loss. The use of melatonin can be a promising strategy for improving the natural reproductive performance of cows suffering from HS.

The identification of genes associated with heat tolerance and their incorporation into the breeding program and the inclusion of THI covariate effects in the selection index should be targeted for genetic evaluation of dairy animals in the hot climate. (Dash et al., 2016). Work towards the creation of climate-resistant breeds can ensure the sustainability of livestock production systems in the future. In addition, efforts to reduce the risk of HS among dairy cows should also include the search for new environmental methods for forecasting HS and modifying the microclimate based on meteorological forecasts. Thanks to these measures, the breeder can prepare and implement appropriate solutions for animal protection in advance (Herbut et al. 2018).

Unfortunately, no single approach can fully ensure the excellent fertility of cows during HS. However, appropriate combinations of strategies can significantly increase the effectiveness of reproductive measures (Negrón-Pérez et al., 2019).

Conclusion

To conclude, the reproductive function of cows under HS is disrupted at various physiological stages (pregnancy, calving, postpartum period), ranging from reduced fertility to reproductive loss and culling of animals. This entails significant financial losses.

For this reason prevention of HS is one of the most important tasks for dairy farm owners during the hot season of the year. The effects of HS on animals can be minimized by appropriate scientific strategies, the adaptation of environment and feeding, and the genetic development of heat-resistant breeds.

Thus, understanding the mechanisms of the negative effects of high temperatures on the reproductive function of productive animals will help in the development of mitigation strategies. The measures to reduce the incidence of mastitis, to use artificial insemination more often and genetic selection of donors for the ability to effectively thermoregulate will be in demand under any climate change scenario. Therefore, a well-considered timely implementation of the HS control strategy will prevent reproductive and hence economic losses in dairy farming.

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