



UDC: 577.1:619(072)

DOI: 10.31548/ujvs.13(4).2022.16-24

Hormonal regulation of the concentration of glucose and its derivatives in the blood of dairy cows during the transit period

Vasyl Vlizlo^{1*}, Dmytro Ostapiv², Marian Simonov³, Walter Baumgartner⁴, Viktor Tomchuk⁵

¹Full Doctor in Veterinary Sciences, Professor. ORCID: <https://orcid.org/0000-0001-8588-5095>.
Stepan Gzhytskyi National University of Veterinary Medicine and Biotechnologies,
79010, 50 Pekarska Str., Lviv, Ukraine

²Full Doctor in Agricultural Sciences, Associate Professor. ORCID: <https://orcid.org/0000-0001-8112-5398>.
Institute of Animal Biology NAAS, 79034, 38 Vasyl Stus Str., Lviv, Ukraine

³Full Doctor in Veterinary Sciences, Associate Professor. ORCID: <https://orcid.org/0000-0001-6691-6773>.
Stepan Gzhytskyi National University of Veterinary Medicine and Biotechnologies,
79010, 50 Pekarska Str., Lviv, Ukraine

⁴Full Doctor in Veterinary Sciences, Professor. ORCID: <https://orcid.org/00000-0001-7366-7242>.
University of Veterinary Medicine Vienna, 1210, 1 Veterinärplatz, Vienna, Austria

⁵Full Doctor in Veterinary Sciences, Professor. ORCID: <https://orcid.org/0000-0001-6601-1392>.
National University of Life and Environmental Sciences of Ukraine,
03041, 15 Heroiv Oborony Str., Kyiv, Ukraine

Abstract. In dairy cows, metabolic disorders are mainly found in the last weeks of the dry period and the first weeks after calving (transit period). Therefore, the purpose of this study was to investigate the hormonal regulation of the concentration of glucose and its derivatives in the blood of dairy cows during the transit period. The study was conducted on cows of 2-4 lactations, with a capacity of 7.8-8.2 thousand kg of milk for previous lactation. Blood for research was taken from cows 7-10 days before calving and Days 2-4, Days 10-14, and Days 30-40 after calving. The concentration of glucose in blood plasma was determined by the glucose oxidase method, pyruvate – by the modified Umbright method, lactate – by reaction with paraoxydyphenyl, and hormone content – by enzyme-linked immunosorbent assay. It was established that high-performance dairy cows during the transit period experience substantial changes in carbohydrate metabolism and the functional state of organs and systems, which are aimed at ensuring high productivity. Thus, hypoglycaemia is found in cows within two weeks after calving. At the same time, with a decrease in the concentration of glucose in the blood plasma of cows, the content of pyruvate and lactate increases, as well as the lactate/pyruvate ratio, which indicates an increase in gluconeogenesis. Negative energy balance and increased gluconeogenesis lead to a decrease in the synthesis of insulin and insulin-like growth factor. Compared to the final dry period, on Days 2-4 of lactation, the concentration of leptin in the blood plasma of cows decreased threefold and stayed at a low level until Day 40 of lactation. Plasma cortisol levels were highest on Days 2-4 and 10-14 of lactation. Intensive cortisol synthesis during the period of energy deficiency increases gluconeogenesis, which is possible due to lipolysis and proteolysis. In the first days after calving, the content of thyroxine and triiodothyronine in the blood plasma of cows decreased. Inhibition of thyroid hormone production is a consequence of the physiological regulatory features of this period. Thus, in highly productive cows during the transit period, attention should be paid to maintaining vital body functions and their well-coordinated endocrine regulation, which will ensure a physiologically balanced metabolic rate, successful calving, high milk productivity, and animal health

Keywords: dairy cattle breeding, carbohydrate metabolism, lactate, pyruvate, hormones

Suggested Citation:

Vlizlo, V., Ostapiv, D., Simonov, M., Baumgartner, W., & Tomchuk, V. (2022). Hormonal regulation of the concentration of glucose and its derivatives in the blood of dairy cows during the transit period. *Ukrainian Journal of Veterinary Sciences*, 13(4), 16-24.

*Corresponding author

Introduction

In recent decades, cow productivity has considerably increased in countries with highly developed dairy cattle breeding (Barkema *et al.*, 2015). Today in Ukraine, dairy productivity has exceeded 6,500 kg on average, and in the best farms it has reached 10,000 kg or more per cow per year (State Statistics..., 2021). A high level of milk productivity requires a sufficient amount of nutrients and vital biologically active substances for the body. Therefore, in highly productive dairy cows in the last weeks before and the first after calving, there is an increase in metabolism (Stivanin *et al.*, 2021). In the specialized literature, this period is called transition (Knob *et al.*, 2021). For highly productive dairy cows, it is the crucial stage that determines the state of their health and the calves born from them, and in general – the level of productivity and profitability of the farm.

In the final stage of pregnancy, the main expenditure of nutrients is spent on fetal growth, placental development, and breast preparation for lactation. After calving, cows lose body weight from the main body depots due to considerable energy needs and insufficient supply of energy deriving from feed. Due to the inability to ensure that the body receives enough energy to cover the body's needs and milk production, highly productive dairy cows have a negative energy balance at the beginning of lactation (Soonberg *et al.*, 2021). In the first days after calving, the lack of energy is first compensated by the breakdown of glycogen in the liver and muscles. However, glycogenolysis quickly fades, since glycogen reserves are enough only for the first two to three days, and with a considerable energy deficiency – even less (Soonberg *et al.*, 2021; Cabezas-Garcia *et al.*, 2021). Therefore, to cover the energy deficit, a highly productive cow uses reserve fats that are deposited during the mobilisation and dry periods.

A slight energy deficit that occurs in cows after childbirth is considered a physiological phenomenon. The milk productivity of cows is maximum in the first two months after calving, but currently the assimilation of basic nutrients from the feed is insufficient to provide them to the body. First of all, an energy deficiency occurs, which causes rapid weight loss and increases the risk of metabolic diseases in animals (Vossebeld *et al.*, 2022). Excessive and prolonged intake of lipids causes insufficient oxidation in the tricarboxylic acid cycle and activation of ketogenesis (Mezzetti *et al.*, 2019). Therefore, with the intensive course of metabolic processes in highly productive cows, even minor management errors on farms cause the development of morbidity, specifically metabolic pathology (Banda *et al.*, 2022; Grala *et al.*, 2022).

Metabolic diseases of cows are a considerable obstacle to increasing productivity in dairy cattle breeding. They lead to significant economic losses in animal husbandry due to a shortfall in offspring and milk, an increase in the cost of production (Van Saun, 2016).

Metabolic disorders in the body of animals often occur subclinically, and therefore are not established in time by livestock breeders and are not diagnosed by veterinary doctors. The study of the content of metabolic indicators in the body of cows during the transit period should be considered when developing a strategy for monitoring metabolic disorders, which is a component of preventive measures against the spread of relevant diseases and early

culling of valuable livestock. Therefore, it is important for specialists working with highly productive dairy cows to consider the patterns of metabolism in the body of healthy animals during the transit period (Smith *et al.*, 2017). This is also important for determining effective means of treating sick animals and timely implementation of preventive measures that would prevent the progression of pathology. At the same time, the negative energy balance and metabolic disorders that occur during the transit period contribute to immunosuppression, which can lead to the development of both internal diseases and infectious pathology (Hailemariam *et al.*, 2014; Lacasse *et al.*, 2018).

Consequently, the state of metabolism in the body of dairy cows during the transit period undergoes significant changes, which are aimed at compensating for increased needs for energy, nutrients, and biologically active substances. The cow's body responds to the negative state of energy balance through compensating for the lack of energy by mobilizing carbohydrates, proteins, and lipids of the body depot (Weber *et al.*, 2013). The conducted literature analysis and earlier studies by authors of the present paper indicate that it is currently important to conduct medical examinations or monitoring studies in dairy farms to establish the main blood parameters that characterize the state of metabolism in cows during the transition period (Simonov & Vlizlo, 2015; Walter *et al.*, 2022).

The purpose of this study was to find the concentration of glucose, pyruvate, and lactate in the blood plasma of dairy cows before calving and in the first weeks of lactation, as well as hormonal regulation and mechanisms of metabolic disorders during this period.

Materials and Methods

The study was carried out per the provisions of the "European Convention for the protection of vertebrates used for experimental and other purposes" (Strasbourg, 1986) (European convention..., 1986) and considering the "General Ethical Principles of Animal Experiments" (Galkin & Grigorenko, 2011), which were adopted by the first National Congress on Bioethics (Ukraine, 2001).

The cows were studied on the farm of the Lviv region, and blood tests were carried out in the laboratory of Molecular Biology and Clinical Biochemistry of the Institute of Animal Biology of the National Academy of Agrarian Sciences and at the Department of Internal Diseases of Animals and Clinical Diagnostics of the Stepan Gzhyskyi National University of Veterinary Medicine and Biotechnologies Lviv during 2020-2021. The object of this study was highly productive cows of the Holstein breed, at various stages of the physiological state and periods of maintenance. The first period of the study concerned cows 7-10 days before calving, the other three periods – after calving: the second – Days 2-4, the third – Days 10-14, and the fourth – Days 30-40. Analogous cows were selected for the study in terms of productivity, body weight, and age. Cows corresponded to 2-4 lactations, with a productivity of 7.8-8.2 thousand kg of milk per previous lactation. Overall, the study was conducted on 80 dairy cows. All animals underwent a daily clinical examination. If sick animals were identified, they were prescribed treatment, depending on the diagnosed pathology. Animals that were treated were not used for further studies.

Blood for research was obtained from the jugular vein of cows, in the morning, before feeding them. The blood was stabilized by adding heparin to the test tubes. After taking blood from cows, plasma was obtained directly on the farm. For this, the blood was immediately centrifuged at 3,000 rpm for 20 minutes. The resulting blood plasma was transferred to chemically clean, dry test tubes, and transported in a portable refrigerator to the laboratory, where it was stored in a stationary refrigerator at +4-6°C and used for analysis (up to three days). The rest of the obtained blood plasma was frozen at -20°C and stored for up to two months before the next analysis. In the blood plasma of cows, glucose concentrations were determined using the glucose oxidase method, pyruvate – according to the modified Umbright method, and lactate – by reaction with paraoxydiphenyl. These studies were performed on a biochemical Evolution 3000 analyser (Italy). The concentration of hormones in the blood plasma (insulin, cortisol, insulin-like growth factor, leptin, thyroid-stimulating hormone, triiodothyronine, thyroxine) was established according to the enzyme immunoassay method using test kits from the companies “Human” (Germany), “DRG” (Germany), and “Orgentec” (Netherlands).

Statistical analysis of blood parameters was performed using a personal computer and Microsoft Excel software. In distinct groups of cows, the arithmetic mean (M) and statistical error of the arithmetic mean (m) were found from the obtained blood parameters. The correlation coefficient (r) was calculated between individual groups and indicators. The probability of differences in values between groups was calculated using the Student’s criterion. Differences were considered significant at $P < 0.05-0.001$. Diagrams in figures were constructed using Excel according to generally accepted algorithms. The figures in this paper contain average values of quantities (M).

Results and Discussion

The concentration of glucose in the blood is the main indicator according to which the level of energy supply to the body is determined. Studies have proved that the low concentration of glucose in the blood plasma of cows (Fig. 1) is recorded in the last 7-10 days before calving (2.5 ± 0.2 mmol/L), while on Days 2-4 and 10-14 after calving, its concentration was marked by the lowest values (2.2 ± 0.1 mmol/L and 2.2 ± 0.1 mmol/L, respectively).

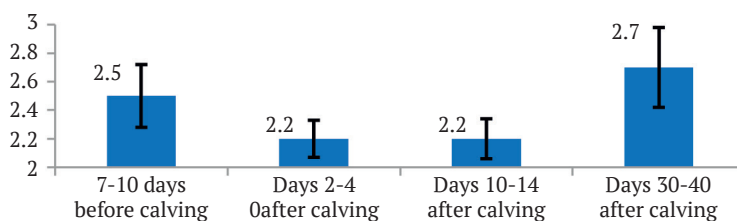


Figure 1. Concentration of glucose in the blood plasma of cows during the transit period, mmol/L

Low plasma glucose concentrations in cows are usually recorded during the first weeks after calving (Vosseveld *et al.*, 2022). Such changes can be considered as a result of a mismatch between energy intake with feed and glucose consumption for metabolic processes and milk synthesis. In healthy, highly productive cows, the need for energy and protein in the first days after calving exceeds their consumption with feed. Therefore, with a shortage of glucose, cows use their lipid reserves from the depot of the body, which causes an increase in the level of non-esterified fatty acids and ketone bodies in the blood (Imhasly *et al.*, 2015). Such changes can cause metabolic disorders, specifically the development of ketosis. Furthermore, glucose is the best fuel for immune cells, so its low concentration during the transition period and high content of ketone bodies can cause immunosuppression (Ingvarstsen & Moyes, 2013) and weaken the body’s defences.

On Days 30-40 after calving, the blood glucose content of cows increased to 2.7 ± 0.3 , or 23% compared to the

first two weeks after calving (Fig. 1). However, in another 40% of animals, its level stayed below the lower limit of physiological fluctuations (2.5-3.5 mmol/L).

Glucose metabolism in body cells depends on access to oxygen. During the oxidation of glucose under aerobic conditions, pyruvate is formed in the body, and when the breakdown occurs without oxygen, glycolysis occurs anaerobically with enhanced formation of lactate. It was found that simultaneously with a decrease in the concentration of glucose in the blood plasma of cows after calving, the content of pyruvate and lactate increases (Figs. 2 and 3), which indicates the activation of metabolic processes both by aerobic and anaerobic pathways.

Thus, on Days 2-4 after calving, the content of pyruvate in the blood plasma of cows was 114.9 ± 4.8 μ mol/L, and lactate – 1.4 ± 0.3 mmol/L, which is 8% and 50% higher, respectively, compared to the period before calving (106.2 ± 4.01 μ mol/L and 0.9 ± 0.2 mmol/L, respectively).

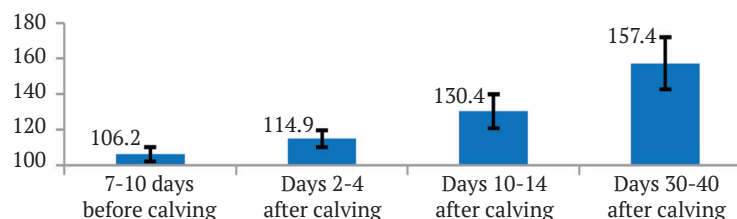


Figure 2. Concentration of pyruvate in the blood plasma of cows during the transit period, μ mol/L

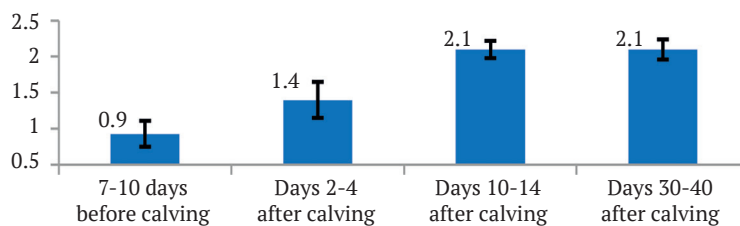


Figure 3. Concentration of lactate in the blood plasma of cows during the transit period, mmol/L

Pyruvate and lactate values increased even more at Days 10-14 and 30-40 of lactation. During these study periods, the concentration of pyruvate in the blood plasma of cows exceeded its value in the prenatal period by 23% ($130.4 \pm 5.3 \mu\text{mol/L}$; $P < 0.01$) and 48% ($157.4 \pm 7.03 \mu\text{mol/L}$; $P < 0.001$), and lactate – by 2.3 times (2.1 ± 0.3 and $2.10 \pm 0.5 \text{ mmol/L}$; $P < 0.001$), respectively. Notably, after

calving, the ratio of lactate to pyruvate in the blood of cows was consistently higher than that of dry cows (Fig. 4), which may indicate an increase in gluconeogenesis processes. Thus, if 7-10 days before calving the ratio of lactate to pyruvate corresponded to 9, then on Days 2-4 after calving it corresponded to 12, on Days 10-14 – to 17, and on Days 30-40 days – to 14.

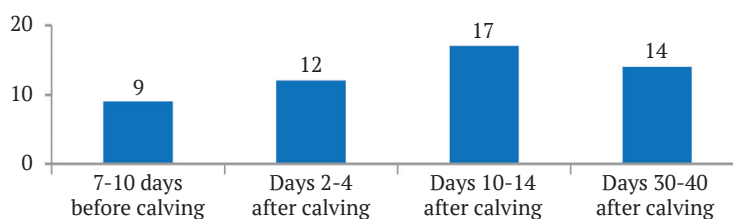


Figure 4. Ratio of lactate to pyruvate in cow blood plasma during the transit period

The metabolism of carbohydrates in the body of ruminants is aimed at maintaining the stability of the concentration of glucose in the blood, including during energy deficit, since the brain feeds exclusively on glucose. Proceeding from this, at the beginning of lactation, when the need for glucose for milk lactose synthesis is high and the supply of glucose precursors from feed is low, activation of gluconeogenesis is a vital compensatory mechanism (Schulz *et al.*, 2014). In ruminants, to provide the body with energy, gluconeogenesis is continuous and increases after feeding. Their need for glucose is provided as a result of gluconeogenesis by 90% or more, which is regulated by the endocrine system (Knob *et al.*, 2021). Thus, in the blood plasma of cows on Days 2-4 after calving, a decrease in the concentration of insulin to $122.8 \pm 16.5 \text{ pmol/L}$ ($P < 0.001$) was found compared

to $260.9 \pm 19.2 \text{ pmol/L}$ in the period of 7-10 days before calving (Fig. 5). On Days 10-14 and 30-40 after calving, the plasma insulin concentration was 163.5 ± 17.7 and $164.6 \pm 15.8 \text{ pmol/L}$, which was 33% and 34% higher, respectively, compared to Days 2-4 ($122.8 \pm 16.5 \text{ pmol/L}$), but even lower by 38% ($P < 0.05$) and 37%, respectively, than in dry animals ($260.9 \pm 19.2 \text{ pmol/L}$). Low insulin concentrations lead to inhibition of glycogenesis and contribute to the support of plasma glucose levels (Vosseveld *et al.*, 2022). In the literature, the reduction of insulin synthesis by the pancreas of dairy cows of the transit period is called insulin resistance (Rico *et al.*, 2015). Insulin resistance is a consequence of the body's metabolic adaptation to energy deficiency. This process increases gluconeogenesis in the liver in cows and reduces glucose uptake by skeletal muscles and other tissues (Spachmann *et al.*, 2013).

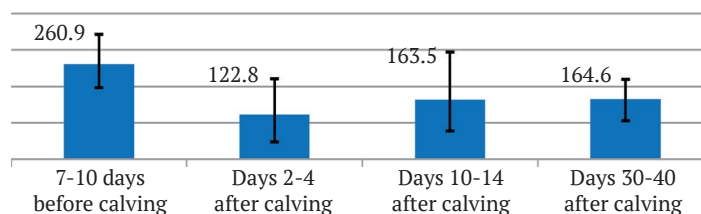


Figure 5. Concentration of insulin in the blood plasma of cows during the transit period, pmol/L

However, insulin resistance accelerates lipolysis during the transition period, and this increases the risk of metabolic diseases in dairy cattle (Rico *et al.*, 2015). Therefore, a decrease in insulin synthesis at the beginning of lactation is probably associated with glucose deficiency and increased gluconeogenesis. Activation of gluconeogenesis increases the mobilization of energy substances from the depot, especially

lipids, which can adversely affect the intensity and direction of metabolism and provoke the development of metabolic pathologies (Weber *et al.*, 2013; Gruber & Mansfeld, 2019). Specifically, increased lipomobilization and the development of excessive amounts of free fatty acids causes functional liver overload and the development of fatty hepatocyte infiltration (Ingvarsen & Moyes, 2013; Imhasly *et al.*, 2015).

The next pathway of physiological metabolism regulation occurs through the activation of the adrenal glands, which produce glucocorticoids, primarily cortisol. The latter induces all key enzymes of gluconeogenesis and provides this process with starting compounds and reduces the need for glucose in tissues, thereby increasing its level in the blood (Ebinghaus *et al.*, 2020). In turn, this helps the

body overcome stress, support a certain level of glucose in the blood, even with insufficient intake of carbohydrates. By stimulating protein breakdown, cortisol promotes the release of amino acids, which are also essential elements of gluconeogenesis. The conducted studies of cortisol concentration in blood plasma of cows indicated (Fig. 6) its highest level on Days 2-4 and 10-14 of lactation.

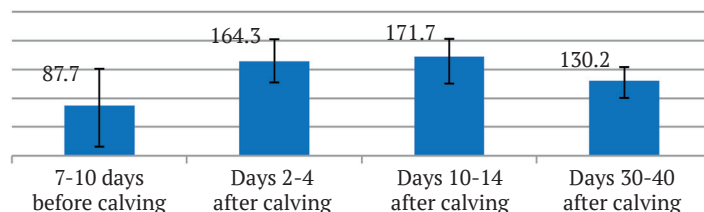


Figure 6. Concentration of cortisol in the blood plasma of cows during the transit period, µIU/L

Thus, the content of cortisol in blood plasma after calving on Days 2-4 was higher by 87% (164.3 ± 17.3 µIU/L; $P < 0.01$), on Days 10-14 – by 96% (171.7 ± 16.9 µIU/L; $P < 0.001$), and on Days 30-40 – by 48% (130.2 ± 14.8 µIU/L; $P < 0.05$) compared to the end of the dry period (87.7 ± 12.4 µIU/L). Increased cortisol synthesis during energy deficiency can enhance gluconeogenesis through lipolysis and proteolysis (Gross *et al.*, 2015).

Apart from insulin and cortisol, markers of metabolism in dairy cows can also be the concentration of insulin-like growth factor (IGF, somatomedin) and leptin in blood plasma (Petruh *et al.*, 2018). Presently, IGF and leptin can be attributed

to understudied hormones. Insulin-like growth factor is synthesized mainly in the liver in response to an increase in the level of somatotrophic hormone in the blood. In its physiological properties, IGF is close to insulin, structurally similar, and has common receptors that trigger the same reaction chains (Simonov *et al.*, 2021). It stimulates the transport of amino acids and glucose in muscles, increases the sensitivity of cells to insulin, while in adipose tissue it promotes the transport of glucose, its oxidation and transformation into lipids (Mollo *et al.*, 2021). That is why the concentration of IGF decreased in the blood of cows after calving (Fig. 7) compared to the dry period.

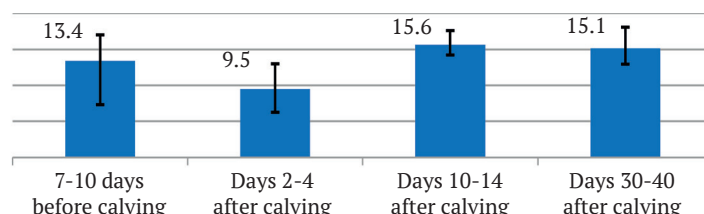


Figure 7. Concentration of insulin-like growth factor (IGF) in cow blood plasma during the transit period, nmol/L

Thus, the concentration of IGF in blood plasma on Days 2-4 days of lactation was 29% lower (9.5 ± 1.5 nmol/L; $P < 0.05$) compared to the period of 7-10 days before calving (13.4 ± 1.3 nmol/L). The correlation between blood insulin concentrations and IGF during the first day after calving is remarkably high ($r = +0.9$). Consequently, when dairy cows develop a negative energy balance after calving and a decrease in blood glucose concentration, the endocrine system inhibits the synthesis of insulin, IGF, and glucagon (Vossebelt *et al.*, 2022; Fazio *et al.*, 2022).

On Days 10-14 after calving, compared to Days 2-4, the concentration of IGF in the blood plasma of cows increased by 64% (15.6 ± 1.4 nmol/L; $P < 0.01$) and stayed at this level until Days 30-40 (15.1 ± 1.7 nmol/L; $P < 0.05$). However, the correlation between IGF and insulin levels on

Days 10-14 after calving was still quite positively high ($r = +0.7$). This suggests that IGF is important in the energy supply of the body of dairy cows.

The tissue hormone leptin is synthesized by adipocytes, and its main physiological function is to reduce the synthesis of macroergic compounds and increase energy expenditure. Circulating in the blood, leptin helps support optimal glucose levels, which are essential for the body's energy needs (Petruh *et al.*, 2018). The results of the conducted studies indicate (Fig. 8) that, compared to the end of the dry period (8.10 ± 0.76 µg/L), on Days 2-4 of lactation, the content of leptin in blood plasma decreased by three times (2.67 ± 0.33 µg/L; $P < 0.001$) and stayed at a low level on Days 10-14 (2.22 ± 0.42 µg/L; $P < 0.001$) and until the Day 40 of lactation (2.30 ± 0.61 µg/L; $P < 0.001$).

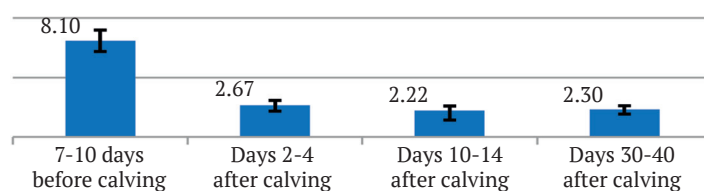


Figure 8. Leptin content in cow blood plasma during the transit period, µg/L

Leptin is involved in the regulation of appetite, interacting with specific receptors located in the hypothalamic region, activates the production of nerve impulses directed to the corresponding areas of the brain. An elevated concentration of leptin in the blood signals that the body has received enough nutrients. Thus, the low content of leptin in the blood plasma of cows after calving established by the results of the study contributes to an increase in feed consumption at the beginning of lactation, when the body's need for nutrients, especially energy, increases considerably.

Thyroid hormones (triiodothyronine, thyroxine) and its main regulator, the pituitary gland, which produces thyroid-stimulating hormone (TSH) play a vital role in the regulation of metabolism in the body of cows, specifically energy metabolism (Fazio *et al.*, 2022). Studies have proved that in comparison with the period of 7-10 days before calving, in the first four days after calving, the concentration of triiodothyronine (T3) decreases (Figs. 9 and 10) in the blood plasma of cows by 54% (from 4.8 ± 0.5 to 2.2 ± 0.3 nmol/L; $P < 0.001$) and thyroxine (T4) – by 35% (from 80.6 ± 6.3 to 52.2 ± 5.0 nmol/L; $P < 0.01$).

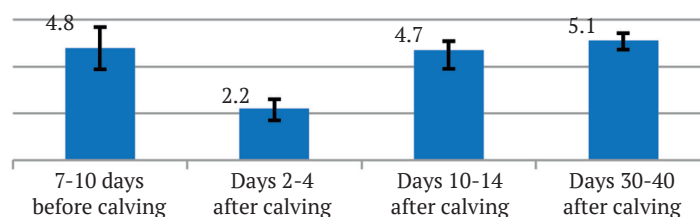


Figure 9. Triiodothyronine concentration (T3) in the blood plasma of cows during the transit period, nmol/L

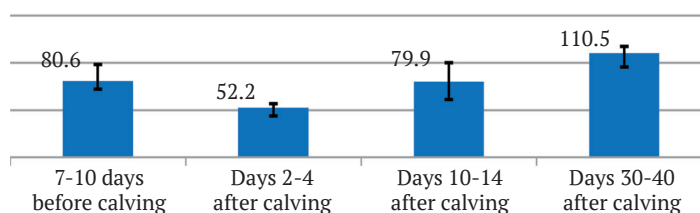


Figure 10. Thyroxine concentration (T4) in the blood plasma of cows during the transit period, nmol/L

At the same time, the study of the concentration of thyroid-stimulating hormone in the blood plasma of cows showed no significant difference (Fig. 11). It was

at the same level (0.21 ± 0.031 and 0.2 ± 0.027 mIU/L, respectively, in the pre-calving period and on Days 2-4 after calving).

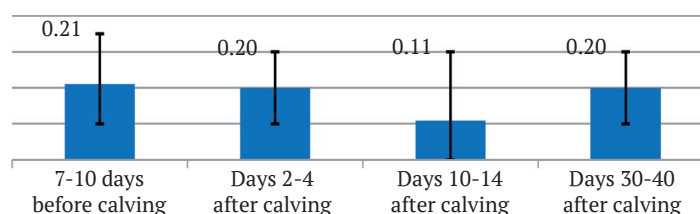


Figure 11. Thyroid-stimulating hormone (TSH) concentration in blood plasma of cows during the transit period, mIU/L

Having conducted the correlation, it was established that on Days 2-4 after calving, it was strongly positive ($r = +0.7$) between the level of thyroxine and insulin-like growth factor, and moderately positive ($r = +0.4$) between the concentration of triiodothyronine and IGF. This may indicate regulatory metabolic processes both in the liver, which produces IGF, and in the thyroid gland. The established low level of IGF and thyroid hormones indicates a decrease in the use of energy compounds by body tissues and increases their availability to the mammary gland. This is one of the mechanisms of energy redistribution in favour of milk formation. This suggests that a decrease in the synthesis of IGF and thyroid hormones is a consequence of the physiological regulatory features of this period. It is indicated that the level of IGF in the blood depends on the concentration of thyroid hormones that increase the secretion of

IGF by the liver (Petruh *et al.*, 2018). Starting from Days 10-14 after calving, compared to Days 2-4 days, the concentration of T3 in the blood plasma of cows increased by 2.1 times (4.7 ± 0.5 nmol/L; $P < 0.001$) and T4 – by 53% (79.9 ± 6.2 nmol/L; $P < 0.01$). On Days 30-40, the concentration of T3 stayed stable (5.1 ± 0.4 nmol/L; $P < 0.001$), while T4 – increased (110.5 ± 9.7 nmol/L; $P < 0.001$) and was the highest for all periods under study (Figs. 9 and 10). The growth of thyroid hormones activates the carbohydrate and protein catabolism, stimulates lipomobilization with a negative energy balance. On Days 10-14 after calving, the correlation between the level of IGF and thyroid hormones was weak ($r = +0.2-0.3$), in contrast to the nature of the correlation between IGF and insulin level ($r = +0.7$).

Thus, the analysis of the literature and research of the authors of the present paper indicate that in

high-yielding dairy cows in the transit period, the state of metabolism, specifically energy metabolism, should be monitored, since even minor deviations can cause its disruption and the development of diseases.

Conclusions

In highly productive dairy cows, in the last weeks before calving and the first weeks of lactation period, there is a considerable increase in energy metabolism, which is aimed at ensuring high productivity. In the first 14 days after calving, the concentration of glucose in the blood plasma of cows decreases to 2.2 ± 0.1 mmol/L, which indicates a lack of energy in the body. Compared to the pre-calving period, during the first 40 days of lactation, the concentration of pyruvate in the blood plasma of cows increases by 48% (157.4 ± 7.03 μ mol/L; $P < 0.001$), and lactate, even by 2.3 times (2.1 ± 0.5 mmol/L; $P < 0.001$), which indicates an increase in the breakdown of carbohydrates, specifically by anaerobic means.

Supporting the physiological course of metabolism in the body of cows of the transit period is actively regulated

by the endocrine system. With a low level of glucose in the blood plasma of dairy cows in the first weeks of lactation, compared to the period before calving, the body produces 37-47% less insulin (122.8 ± 16.5 - 164.6 ± 15.8 pmol/L; $P < 0.001$ - $P < 0.05$) and leptin by 3.0-3.5 times (2.67 ± 0.33 - 2.30 ± 0.61 μ g/L; $P < 0.001$), and in the first 4 days also insulin-like growth factor by 29% (9.5 ± 1.5 nmol/L; $P < 0.05$) and increases the synthesis of cortisol from 48% to 96% (130.2 ± 14.8 - 171.7 ± 16.9 μ IU/L; $P < 0.05$ - 0.001), and from 10 to 40 days – triiodothyronine (5.1 ± 0.4 nmol/L; $P < 0.001$) and thyroxine (110.5 ± 9.7 nmol/L; $P < 0.001$), which contributes to the stabilization of energy metabolism. Therefore, in the transit period, a well-coordinated regulatory action on the part of the endocrine system is important, which would ensure the completion of pregnancy, successful calving, high milk yield due to increased activity and support of metabolic intensity at the physiological level.

Further research will relate to the investigation of metabolic pathology, elucidation of aetiological factors, and pathogenetic mechanisms of metabolic diseases in dairy cows in the first weeks after calving.

References

- [1] Banda, L., Chagunda, M., Ashworth, C., & Roberts, D. (2022). Associations among body energy status, feeding duration and activity with respect to diet energy and protein content in housed dairy cows. *Journal of Dairy Research*, 89(2), 128-133. doi: 10.1017/S0022029922000267.
- [2] Barkema, H.W., von Keyserlingk, M.A., Kastelic, J.P., Lam, T.J., Luby, C., Roy, J.P., LeBlanc, S.J., Keefe, G.P., & Kelton, D.F. (2015). Changes in the dairy industry affecting dairy cattle health and welfare. *Journal of Dairy Science*, 98(11), 7426-7445. doi: 10.3168/jds.2015-9377.
- [3] Cabezas-Garcia, E.H., Gordon, A.W., Mulligan, F.J., & Ferris, C.P. (2021). Revisiting the relationships between fat-to-protein ratio in milk and energy balance in dairy cows of different parities, and at different stages of lactation. *Animals*, 11(11), article number 3256. doi: 10.3390/ani11113256.
- [4] Ebinghaus, A., Knierim, U., Simantke, C., Palme, R., & Ivemeyer, S. (2020). Fecal cortisol metabolites in dairy cows: A cross-sectional exploration of associations with animal, stockperson, and farm characteristics. *Animals*, 10(10), article number 1787. doi: 10.3390/ani10101787.
- [5] European convention for the protection of vertebrate animals used for experimental and other scientific purposes. (1986, March). Retrieved from https://zakon.rada.gov.ua/laws/show/994_137.
- [6] Fazio, E., Bionda, A., Chiofalo, V., Crepaldi, P., Lopreato, V., Medica, P., & Liotta, L. (2022). Adaptive responses of thyroid hormones, insulin, and glucose during pregnancy and lactation in dairy cows. *Animals*, 12(11), article number 1395. doi: 10.3390/ani12111395.
- [7] Galkin, O.Yu., & Grigorenko, A.A. (2011). Bioethics in Ukraine: From theory to practice. Normative-legal and educational-scientific aspects. *Research Bulletin of the National Technical University of Ukraine "Kyiv Polytechnic Institute"*, 3, 12-19.
- [8] Grala, T.M., Kuhn-Sherlock, B., Roche, J.R., Jordan, O.M., Phyn, C.V.C., Burke, C.R., & Meier, S. (2022). Changes in plasma electrolytes, minerals, and hepatic markers of health across the transition period in dairy cows divergent in genetic merit for fertility traits and postpartum anovulatory intervals. *Journal of Dairy Science*, 105(2), 1754-1767. doi: 10.3168/jds.2021-20783.
- [9] Gross, J.J., Wellnitz, O., & Bruckmaier, R.M. (2015). Cortisol secretion in response to metabolic and inflammatory challenges in dairy cows. *Journal of Animal Science*, 93(7), 3395-3401. doi: 10.2527/jas.2015-8903.
- [10] Gruber, S., & Mansfeld, R. (2019). Herd health monitoring in dairy farms – Discover metabolic diseases. *Tierärztliche Praxis*, 47(4), 246-255. doi: 10.1055/a-0949-1637.
- [11] Hailemariam, D., Mandal, R., Saleem, F., Dunn, S.M., Wishart, D.S., & Ametaj, B.N. (2014). Identification of predictive biomarkers of disease state in transition dairy cows. *Journal of Dairy Science*, 97(5), 2680-2693. doi: 10.3168/jds.2013-6803.
- [12] Imhasly, S., Bieli, C., Naegeli, H., Nyström, L., Ruetten, M., & Gerspach, C. (2015). Blood plasma lipidome profile of dairy cows during the transition period. *BMC Veterinary Research*, 11, article number 252. doi: 10.1186/s12917-015-0565-8.
- [13] Ingvarstsen, K.L., & Moyes, K. (2013). Nutrition, immune function and health of dairy cattle. *Animal*, 7(1), 112-122. doi: 10.1017/S175173111200170X.
- [14] Knob, D.A., Thaler Neto, A., Schweizer, H., Weigand, A.C., Kappes, R., & Scholz, A.M. (2021). Energy balance indicators during the transition period and early lactation of purebred Holstein and Simmental cows and their crosses. *Animals*, 11(2), article number 309. doi: 10.3390/ani11020309.
- [15] Lacasse, P., Vanackerab, N., Olliera, S., & Sterab, C. (2018). Review: Innovative dairy cow management to improve resistance to metabolic and infectious diseases during the transition period. *Research in Veterinary Science*, 116, 40-46. doi: 10.1016/j.rvsc.2017.06.020.

- [16] Mezzetti, M., Minuti, A., Piccioli-Cappelli, F., Amadori, M., Bionaz, M., & Trevisi, E. (2019). The role of altered immune function during the dry period in promoting the development of subclinical ketosis in early lactation. *Journal of Dairy Science*, 102(10), 9241-9258. doi: 10.3168/jds.2019-16497.
- [17] Mollo, A., Agazzi, A., Prandi, A., Fusi, J., De Amicis, I., & Probo, M. (2021). Metabolic and production parameters of dairy cows with different dry period lengths and parities. *Acta Veterinaria Hungarica*, 69(4), 354-362. doi: 10.1556/004.2021.00049.
- [18] Petruh, I., Simonov, M., Vlizlo, V., & Ostapiv, D. (2018). The role of insulin-like growth factor and leptin in the pathogenesis of internal non-contagious pathology of dairy cows. *Ukrainian Journal of Veterinary and Agricultural Sciences*, 1(2), 19-22. doi: 10.32718/ujvas1-2.05.
- [19] Rico, J.E., Bandaru, V.V.R., Dorskind, J.M., Haughey, N.J., & McFadden, J.W. (2015). Plasma ceramides are elevated in overweight Holstein dairy cows experiencing greater lipolysis and insulin resistance during the transition from late pregnancy to early lactation. *Journal of Dairy Science*, 98(11), 7757-7770. doi: 10.3168/jds.2015-9519.
- [20] Schulz, K., Frahm, J., Meyer, U., Kersten, S., Reiche, D., Rehage, J., & Dänicke, S. (2014). Effects of prepartal body condition score and peripartal energy supply of dairy cows on postpartal lipolysis, energy balance and ketogenesis: An animal model to investigate subclinical ketosis. *Journal of Dairy Research*, 81(3), 257-266. doi: 10.1017/S0022029914000107.
- [21] Simonov, M., & Vlizlo, V. (2015). Some blood markers of the functional state of liver in dairy cows with clinical ketosis. *Bulgarian Journal of Veterinary Medicine*, 18(1), 74-82. doi: 10.15547/bjvm.814.
- [22] Simonov, M., Vlizlo, V., Stybel, V., Peleno, R., Salata, V., Matviishyn, T., Khimych, M., & Gorobei, O. (2021). Levels of the etiological factor of cancer insulin-like growth factors in bovine, goat, and sheep milk in different lactation periods. *International Journal of One Health*, 7(2), 246-250. doi: 10.14202/IJOH.2021.246-250.
- [23] Smith, G.L., Friggens, N.C., Ashworth, C.J., & Chagunda, M.G.G. (2017). Association between body energy content in the dry period and post-calving production disease status in dairy cattle. *Animal*, 11(9), 1590-1598. doi: 10.1017/S1751731117000040.
- [24] Soonberg, M., Kass, M., Kaart, T., Barraclough, R., Haskell, M.J., & Arney, D.R. (2021). Effect of grouping on behaviour of dairy heifers and cows in the transition period. *Journal of Dairy Research*, 88(1), 45-51. doi: 10.1017/S0022029921000066.
- [25] Spachmann, S.K., Schönhusen, U., Kuhla, B., Röntgen, M., & Hammon, H.M. (2013). Insulin signaling of glucose uptake in skeletal muscle of lactating dairy cows. In J.W. Oltjen, E. Kebreab, H. Lapierre (Eds.), *Energy and protein metabolism and nutrition in sustainable animal production* (pp. 277-278). Wageningen: Academic Publishers. doi: 10.3920/978-90-8686-781-3_92.
- [26] Official website of the State Statistics Service of Ukraine. (n.d.). Retrieved from <http://www.ukrstat.gov.ua>.
- [27] Stivanin, S.C.B., Vizzotto, E.F., Matiello, J.P., Machado, F.S., Campos, M.M., Tomich, T.R., Pereira, L.G.R., & Fischer, V. (2021). Behavior, feed intake and health status in Holstein, Gyr and Girolando-F1 cows during the transition period: Behavior and health of dairy cows in the transition period. *Applied Animal Behaviour Science*, 242, article number 105403. doi: 10.1016/j.applanim.2021.105403.
- [28] Van Saun, R.J. (2016). Indicators of dairy cow transition risks: Metabolic profiling revisited. *Tierärztliche Praxis*, 44(2), 118-126. doi: 10.15653/TPG-150947.
- [29] Vossebeld, F., van Knegsel, A.T.M., & Saccenti, E. (2022). Phenotyping metabolic status of dairy cows using clustering of time profiles of energy balance peripartum. *Journal of Dairy Science*, 105(5), 4565-4580. doi: 10.3168/jds.2021-21518.
- [30] Walter, L.L., Gärtner, T., Gernand, E., Wehrend, A., & Donat, K. (2022). Effects of parity and stage of lactation on trend and variability of metabolic markers in dairy cows. *Animals*, 12(8), article number 1008. doi: 10.3390/ani12081008.
- [31] Weber, C., Hametner, C., Tuchscherer, A., Losand, B., Kanitz, E., Otten, W., Singh, S.P., Bruckmaier, R.M., Becker, F., Kanitz, W., & Hammon, H.M. (2013). Variation in fat mobilization during early lactation differently affects feed intake, body condition, and lipid and glucose metabolism in high-yielding dairy cows. *Journal of Dairy Science*, 96(1), 165-180. doi: 10.3168/jds.2012-5574.

Гормональна регуляція концентрації глюкози та її похідних у крові молочних корів під час транзитного періоду

**Василь Васильович Влізло¹, Дмитро Дмитрович Остапів²,
Маріан Романович Сімонов³, Вальтер Баумгартнер⁴, Віктор Анатолійович Томчук⁵**

¹Доктор ветеринарних наук, професор. ORCID: <https://orcid.org/0000-0001-8588-5095>.
Львівський національний університет ветеринарної медицини та біотехнологій імені С. З. Гжицького,
79010, вул. Пекарська, 50, м. Львів, Україна

²Доктор сільськогосподарських наук, доцент. ORCID: <https://orcid.org/0000-0001-8112-5398>.
Інститут біології тварин НААН,
79034, вул. Василя Стуса, 38, м. Львів, Україна

³Доктор ветеринарних наук, доцент. ORCID: <https://orcid.org/0000-0001-6691-6773>.
Львівський національний університет ветеринарної медицини та біотехнологій імені С. З. Гжицького,
79010, вул. Пекарська, 50, м. Львів, Україна

⁴Доктор ветеринарних наук, професор. ORCID: <https://orcid.org/00000-0001-7366-7242>.
Університет ветеринарної медицини у Відні,
1210, площа Ветеринарна, 1, м. Відень, Австрія

⁵Доктор ветеринарних наук, професор. ORCID: <https://orcid.org/0000-0001-6601-1392>.
Національний університет біоресурсів і природокористування України,
03041, вул. Героїв Оборони, 15, м. Київ, Україна

Анотація. Порушення обміну речовин у молочних корів переважно реєструють в останні тижні сухостійного періоду та перші – після отелення (транзитний період). Метою роботи було дослідити гормональну регуляцію концентрації глюкози та її похідних у крові молочних корів під час транзитного періоду. Дослідження проводили на коровах 2–4 лактацій, продуктивністю 7,8–8,2 тис. кг молока за попередню лактацію. Кров для досліджень відбирали в корів за 7–10 дів до отелення та на 2–4 добу, 10–14 та 30–40 доби після нього. Концентрацію у плазмі крові глюкози визначали глюкозооксидазним методом, пірувату – модифікованим методом Умбрайта, лактату – за реакцією з параоксидифенілом, а вміст гормонів – методом імуноферментного аналізу. Встановлено, що у високопродуктивних молочних корів під час транзитного періоду відбуваються істотні зміни в обміні вуглеводів та функціонального стану органів і систем, які спрямовані на забезпечення високої продуктивності. Так, у корів упродовж двох тижнів після отелення реєструється гіпоглікемія. Водночас зі зменшенням концентрації глюкози у плазмі крові корів зростає вміст пірувату та лактату, а також відношення лактату до пірувату, що свідчить про посилення глюконеогенезу. Негативний енергетичний баланс та посилення глюконеогенезу призводять до зниження синтезу інсуліну та інсуліноподібного фактору росту. Порівняно із завершальним періодом сухостою, на 2–4 добу лактації, концентрація лептину в плазмі крові корів зменшувалася втричі та трималася на низькому рівні до 40 доби лактації. Рівень кортизолу в плазмі крові був найвищим на 2–4 та 10–14 добу лактації. Інтенсивний синтез кортизолу в період енергетичного дефіциту посилює глюконеогенез, що можливе за рахунок ліполізу та протеолізу. У перші доби після отелення у плазмі крові корів зменшувався вміст тироксину та трийодтироніну. Пригнічення продукції тиреоїдних гормонів є наслідком фізіологічних регуляторних особливостей цього періоду. Таким чином, у високопродуктивних корів під час транзитного періоду слід звертати увагу на підтримання життєво важливих функцій організму та їх злагоджену ендокринну регуляцію, що забезпечить фізіологічно збалансований рівень метаболізму, успішне отелення, високу молочну продуктивність та здоров'я тварин

Ключові слова: молочне скотарство, метаболізм вуглеводів, лактат, піруват, гормони