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# EFFECT OF HYPERPROLACTINEMIA IN ANIMAL PRODUCTION – A REVIEW*

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**Abbreviations: CNS – central nervous system, DOPA – dihydroxyphenylalanine, HP-DKP – histidine-proline diketopiperazine, GABA-γ – gamma-aminobutyric acid, GnRH – gonadotropin-releasing hormone, LUF – luteinized unruptured follicle, PAF – persistent anovulatory follicles, PHDA – periventricular-hypophyseal dopaminergic neurons, PRL – prolactin, PIF – prolactin inhibiting factor, REM – rapid eye movement, SCN – suprachiasmatic nuclei, THDA – tuberohypophyseal dopaminergic neurons, TIDA – tuberoinfundibular dopaminergic neurons, TRH – thyrotrophic releasing hormone, VIP – vasoactive intestinal peptide.**

*Hyperprolactinemia is a hormonal dysfunction that may have physiological, pathological, functional and pharmacological origin. Hyperprolactinemia describes the state of prolonged elevated levels of prolactin, exceeding the physiological norm adopted for a given species. This particular dysfunction is well known in humans. High concentrations of prolactin are also the cause of false pregnancy. In mares, it is the likely cause of fertility problems. Irregularities in ovarian cycles in turn mean difficulties in determining the best timings for artificial insemination and natural mating. Due to the large number of prolactin isoforms, laboratory methods for prolactin level measurement may lead to falsified results, and thus also to misdiagnosis. Drug treatment consists in administration of D2 receptor agonists. Despite the research conducted, the treatment of hyperprolactinemia is not simple, and the disease results in financial losses incurred by animal farmers.*

*Key words: hyperprolactinemia, PRL, fertility*

Hormonal disorders are dysfunctions that can remain undiagnosed in living organisms for a long time, until the onset of visible symptoms (Ahuja et al., 2008). The endocrine system is a complex and tightly coordinated structure that secretes

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hormones in a specific secretion pattern. Elements of the endocrine system mutually control each other; this control is mediated by positive and negative feedback circuits. A primary role in controlling the functioning of the endocrine system is played by the hypothalamus and pituitary. Prolactin (PRL) is a hormone particularly important for lactation maintenance in female mammals (Molik et al., 2010). Increased secretion of prolactin occurs also in other situations: as a result of organic and mental stresses on the body, during copulation, when nipples are stimulated, after a hearty meal, in REM (rapid eye movement) sleep (Brody and Kruger, 2006). The condition in which prolactin levels exceed the established standard limits is called hyperprolactinemia. Hormonal disorders related to enormous prolactin level often cause problems with pregnancy. The sexual cycle remains under the control of a number of factors, and changes in prolactin levels probably also affect its course (Misztal et al., 2005). High concentration of PRL causes the inhibition of GnRH (gonadotropin-releasing hormone) secretion, which in turn leads to decreased concentration of testosterone and progesterone. This situation leads to irregularities in the ovarian cycle (McCue and Squires, 2002). As a consequence, the incorrect determination of the date of ovulation, and the ensuing ineffective natural mating or artificial insemination are a serious obstacle in the process of production intensification.

**Physiological role of prolactin**

The reproductive cycle consists of cyclical changes in reproductive behavior of female animals, often associated with seasonal changes in the environment, under the influence of hormones and closely related to the time of maturation of the ovum and ovulation. Prolactin (PRL) is a peptide hormone composed of amino acids forming a single polypeptide chain. Prolactin secretion occurs in eosinophilic lactotropic cells of the anterior pituitary gland; presence of prolactin and its receptors has also been detected in the neurohypophysis and some structures of the limbic system, such as the amygdala, hypothalamus and hippocampus (Gregory et al., 2000). In addition, prolactin is produced by cells of the immune system, placenta and the myometrium membrane. The source of PRL synthesis may also be some cancer cells (Brody and Kruger, 2006). Process of prolactin secretion is mediated by the hypothalamus, which is the main control structure for this phenomenon. At this stage, we observe a negative feedback circuit at work. Intensity of PRL secretion depends on changes in concentration of this hormone. Control of PRL synthesis and secretion processes is mediated by substances originating in the CNS. A stimulatory effect on PRL-secreting lactotrophs is exhibited by angiotensin II, TRH and VIP. Also oxytocin, bradykinin, bombesin and neurotensin enhance PRL secretion. In the case of substances suppressing the secretion of PRL (PIF – Prolactin Inhibiting Factor), special attention should be paid to a neurotransmitter from the group of catecholamines, synthesized in dopaminergic neurons. Synthesis and secretion of dopamine occurs in the region of the hypothalamus. The control mechanism of PRL by DOPA is already well known. The source of dopamine are dopaminergic neurons located in the brain, in the regions of the paraventricular and arcuate nuclei. They produce dopamine, which then reaches the pituitary. Paraventricular nucleus contains periventricular-hypophyseal dopaminergic (PHDA) neurons, while the arcuate nucleus – tuberohypophyseal dopaminergic (THDA) neu-

rons, as well as tuberoinfundibular dopaminergic (TIDA) neurons. Dopamine produced in TIDA neurons is the main controller of PRL secretion. The produced dopamine diffuses away from the terminals, and is transported by portal blood to anterior pituitary cells. The cell membrane of lactotrophs contains dopamine receptors D2, which bind the dopamine molecules (Freeman et al., 2000). The presence of dopamine receptors D1 and D2 is found in cell membrane of ovarian follicle granulosa cells, and ovarian germinal epithelium. Substances which suppress the secretion of PRL independently of dopamine are produced in the hypothalamus, and include regulatory protein GAP, histidine-proline diketopiperazine (HP-DKP) and gamma-aminobutyric acid (GABA). In the case of peripheral regulation of PRL production and secretion, the major role is played by thyroid hormones and ovarian steroid hormones. These hormones affect prolactin gene transcription, inhibited by triiodothyronine (T3). In the case of estrogens, their activity causes an increase in the number of lactotropic cells of the pituitary, as well as enhanced sensitivity of lactotrophs to TRH and DOPA (Thompson et al., 1986).

**Seasonal rhythm of prolactin**

Prolactin is a hormone whose presence is necessary for correct progression of processes related to preparation of the female's body for rearing of offspring. It is responsible for mammogenesis (development and maturation of the mammary gland), lactogenesis (initiation of lactation) and galactopoiesis (maintenance of milk production). During the feeding of offspring, stimulation of the mammary gland during suckling boosts the secretion of prolactin. The generated nerve impulses reach the CNS, and affect the neuro-secretory nuclei located in the hypothalamus. Through neurotransmitters, stimuli reach the pituitary, resulting in suppression or an increase in PRL secretion. Periodic and circadian changes in prolactin levels are significantly affected by exogenous factors. Intensity of PRL secretion is strongly associated with changes in levels of melatonin produced by the pineal gland. Studies on sheep showed that prolactin is subject to both circadian and yearly rhythms. The controller of circadian changes in prolactin concentration is the oscillator located in the SCN (suprachiasmatic nucleus of the hypothalamus). These changes are impacted also by the pineal gland, as in pinealectomized animals no increase in PRL secretion at the end of the day was found. Additionally, the daily prolactin rhythm is influenced by the dopaminergic system. The weakening of this system is a prerequisite for increases in PRL levels generated under the influence of melatonin. It is important to note that the prolactin circadian rhythm is dependent on the season. In the spring, prolactin concentration is highest at the beginning and end of the photoperiod (dusk-dawn). In the summer, the peak occurs in the middle of the dark phase, while the autumn high values are observed in the mid-morning and late in the day. In winter the circadian changes in prolactin concentration are not statistically significant (Misztal et al., 1997).

In sheep, it has been shown that shortening days lead to a decrease in PRL secretion. Persistence of high concentrations of melatonin in such conditions has pro-gonadotropic effects, which stimulates also ovarian activity. In ovariectomized sheep, infusions of melatonin showed stimulating affects on PRL secretion despite the

absence of estradiol. This may indicate that PRL secretion is independent of steroid hormone secretion (Misztal et al., 2005). In short-day animals, a long dark phase (>10 h/day) causes a decrease in prolactin secretion. Simulating this effect of short--day season through long-term administration of exogenous melatonin reduces the secretion of prolactin in hamsters. In sheep subjected to artificially shortened dark phase (4–8 h/day), no increase in synthesis of PRL was noted. In the case of sheep, studies have shown that changes in length of the dark and light phases significantly affect PRL concentration and milk production. Despite this fact, the use of artificial lighting programs does not result in maintenance of high prolactin concentration and prolongation of lactation (Molik et al., 2007). Changes in levels of prolactin in the blood and pituitary gland of mares are dictated by signals arriving from the environment. An important role is played by factors such as changes in day-length and ambient temperature. PRL levels increase during the breeding season; high concentration of PRL in the blood persists from May to August, while in autumn and winter the PRL concentration is at the low end of the spectrum (Worthy et al., 1987). Studies involving implantation of mares with implants containing exogenous melatonin demonstrated that this hormone has a suppressive effect on prolactin secretion only during certain seasons. Melatonin released from the implant did not have a statistically significant effect on annual changes in concentration of this hormone in the animal blood (Fitzgerald et al., 2000). The impact of exogenous melatonin on changes in PRL level was evident in the spring and summer, when even with short-term administration of melatonin the PRL levels were decreasing. No inhibitory effect of melatonin on PRL secretion was noted in the case of long-term administration of melatonin. Persistently high levels of melatonin are not treated by the organism as a signal that informs about changing length of the photoperiod. Hence what really matters is not so much the concentration of melatonin itself, but its fluctuations. In the case of continuous administration of exogenous melatonin there is no natural stimulus which provides information on the elongating dark phase. It is posited that sensitivity of the prolactin axis to changes in melatonin concentration varies depending on the season (Fitzgerald et al., 2000).

**The role of prolactin in the reproductive cycle**

Effect of prolactin on mammalian organisms is best observed through its impact on the mammary gland. PRL is essential for the development of the gland itself, and later required to initiate and maintain lactation. The presence of this hormone is a prerequisite in over 300 processes that require PRL for their normal progression. Prolactin has a role to play in the functioning of the immune system, in regulating sexual behavior, onset of the maternal instinct. In addition, it is involved in the process of angiogenesis, control of the water-electrolyte balance and phenomena of steroidogenesis and folliculogenesis. Without prolactin, maintenance of the function of the corpus luteum is impossible in the case of swine or certain species of rodents (Harris et al., 2004). The main function of prolactin in mammals is its impact on the course of processes such as mammogenesis, lactogenesis and galactopoiesis. It was experimentally demonstrated that in the case of cows, sheep and pigs, reduced concentration of PRL blocks the completion of mammogenesis and lactogenesis. In cows, increase in

prolactin level is a condition for reaching maximum milk yield in the prenatal period (Akers, 1985).

Prolactin affects the target cells through prolactin receptors – the presence of these receptors has been recorded in the ovaries of sheep, swine, mice and rats. The division of PRL receptors depends on the number of amino acids in a molecule. Prolactin is not a homogeneous hormone, but occurs in various isoforms. Each isoform affects the target cells by binding to its appropriate receptor. Thus the isoform "little" binds to the receptor PRLr-RS, the form "big" – to the receptor PRLr-RI, and the form "big-big" to PRLr-RL. Presence of numerous receptors PRLr-RL and PRLr-RI was found in the ovaries of sheep. It is worth noting that the presence of these structures in large quantities was also detected in stromal cells of primordial follicles and primary follicles, as well as granulosa cells of prenatal follicles and luteal cells. In the cells of the theca layer and granulosa cells of follicles in the antral to gonadotropin-dependent stages, receptors of both long and short isoforms are present in smaller quantities. No presence of these receptors in mural granulosa cells has been noted (Eftekhari and Mohammadalizadeh, 2009). The signal generated by the binding of prolactin molecules to their receptors is not equally strong for all isoforms. The most intense effects are exhibited by molecules binding to long-form receptors. It is hypothesized that the process of folliculogenesis in rodents is largely dependent on the binding of PRL molecules to PRLr-RL receptors. Short PRL isoform exerts a strong influence on the course of processes such as formation of the corpus luteum and maintenance of its functions (Kinoshita et al., 2001; Olazabal et al., 2000; Jöchle, 1997).

In rats, sheep and dogs, PRL-RS exhibits luteotropic effects. Progesterone production by the corpus luteum and maintenance of pregnancy is possible only with sufficient concentration of prolactin in the body. Prolactin also plays a vital role in embryo implantation in women. Prolactin and prostaglandin PGF2α are hormones that have opposite effects on the function of the corpus luteum – prolactin stimulates the production of progesterone by the CL, while prostaglandin has a suppressive effect on this process. It is explained by the fact that PRL stimulates activity of the gene responsible for production of progesterone, whereas PGF2α suppresses this very factor. It has also been demonstrated that prostaglandin in female rats in the final stages of pregnancy inhibits expression of receptor protein of the long and short PRL isoforms in the corpus luteum. Ovulation is associated with bursting of the ovarian follicle wall, which is necessary to release the egg. There are certain factors whose activity leads to rupturing of the connective tissue making up the sheath of the follicle. A correlation between the activity of gonadotropic hormones and production of proteolysis enzymes responsible for ovulation has been identified. Inhibitory effect of PRL on ovulation might be of a direct or indirect nature. In the case of the former, generation of ovarian plasma is inhibited, while in the latter, indirect case, the synthesis of P450 aromatase is inhibited, which in turn leads to suppression of estradiol production in follicular granulosa cells (Stocco et al., 2003).

Effects of prolactin on mature preovulatory follicles is manifest in the correlation between PRL and plasma α2 concentrations in the alveoli. This fact allows to posit that prolactin has a regulating effect on the process of plasma α2 production in the ovary (Yoshimura et al., 1994).

**Physiological conditions of hyperprolactinemia**

Hyperprolactinemia is a condition of hormonal origin, which describes the state of prolonged elevated levels of PRL, exceeding the physiological norm adopted for the given species. The diagnostic values defined for this disease are an increase in hormone levels above 20 ng/ml in women and above 15 ng/ml in men. Prolactin concentration in a human body does not remain constant, but is subject to natural, physiological changes. PRL levels increase in the neonatal period, during sleep, pregnancy, lactation. Content of prolactin in blood serum becomes elevated during stress (physical effort, hypoglycemia). Intensive synthesis and secretion of PRL was also observed during nipple and breast stimulation, as well as copulation (Kałużny and Bolanowski, 2005).

Where the elevated prolactin levels persist (pathologically), it is often indicative of lesions in central nervous system structures. In some cases, hyperprolactinemia may be caused by tumors in the hypothalamic-pituitary region, affecting the secretion of dopamine. Pituitary neoplasms have the capacity to produce PRL (prolactin); in the case of mixed tumors also other pituitary hormones – in addition to prolactin – are secreted, resulting in the so-called organic hyperprolactinemia. Presence of neoplasms of the latter group results in very high concentration of prolactin, in excess of 200 ng/ml. In humans, the aforementioned tumors are diagnosed on the basis of tests, such as nuclear magnetic resonance imaging (MRI) or high-resolution computer tomography scans (CT) (Hadad and Wieck, 2004).

Hyperprolactinemia is more frequently identified in females – studies have shown that for every 20 cases of the disease, 19 are diagnosed in females. The reason for more frequent detection of prolactin in women are the observable clinical symptoms, and not the truly greater incidence of organic hyperprolactinemia in women (Kałużny and Bolanowski, 2005). Persistent chronically high levels of PRL in males result in the weakening of libido and sexual potency – observed in 90% of male subjects with hyperprolactinemia. In 30% of cases diagnosed in males, the disease also gives symptoms in the form of gynecomastia and galactorrhea. Large-sized tumors in the hypothalamic-pituitary region might also press on the optic chiasm, the symptoms of which are headaches and visual field deficits. Symptoms exhibited due to hyperprolactinemia are associated with secondary hypogonadotropic, hypogonadism. The mechanism of onset of hypogonadism is not fully understood; the probable cause might be the elevated levels of endogenous opioids – which have a suppressive effect on the secretion of GnRH – observed in individuals suffering from hyperprolactinemia. The evidence suggesting a crucial role of opioids in emergence of hypogonadism is the fact that women with hyperprolactinemia after administration of the opioid antagonist, naloxone, experience return of their menses. In individuals with hyperprolactinemia, we observe weakened action of estradiol on the pituitary gland, resulting in a decrease in the intensity of cyclical changes in LH concentration. Pre-ovulatory secretion of luteinizing hormone is reduced. As a result of decline in production of estradiol in the ovaries, concentration of this hormone in the blood of females decreases as well. Reduced testosterone levels were, on the other hand, noted in males with hyperprolactinemia. Most of the symptoms associated with increased production of PRL are also linked to hypogonadism.

Hypogonadism is a consequence of hyperprolactinemia, and is associated with abnormal menstruation in women, with infertility in both sexes, as well as rapid loss of bone mass. Individuals with hyperprolactinemia exhibit behaviors similar to those that occur during menopause and accompany psychological disorders. In rare cases, symptoms include hypotrophy or paradoxical hypertrophy of the testis. Another symptom of hyperprolactinemia is the LUF syndrome (luteinized unruptured follicle syndrome), which is the cause of infertility in women (Ruvalcaba et al., 1992). The phenomenon of luteinization of unruptured follicles consists in the egg not being released from a mature follicle. Depending on the case, such a situation may be incidental only or apply to all cycles, which results in infertility. The LUF syndrome is not treated as a disorder unless it concerns more than 10% of the cycles. The syndrome can have many causes, and is often linked to hyperprolactinemia. Women with LUF show greater sensitivity to stress factors. When thyroliberin was administered to patients with LUF, a particularly strong increase in PRL concentration in response to TRH was observed (Kugu et al., 1991). A similar condition known as PAF (persistent anovulatory follicles) occurs in about 8% of mares, although the etiology of this phenomenon is still not entirely clear.

The problem of hyperprolactinemia in bitches is well recognized. More than 80% of the females exhibit lactomania, an atavistic phenomenon (McCue and Squires, 2002). In females of this species, prolactin levels during false pregnancy significantly exceed 4 ng/l. Hormonal changes that occur in the body of a "truly" pregnant female are very similar to those observed in non-pregnant females, resulting in the occurrence of pseudo-pregnancy and very strong maternal instinct. Low levels of progesterone persisting during lactation result – by way of a negative feedback circuit – in more than quadrupled (from 4 ng/ml to 17 ng/ml) PRL concentration (Chavatte-Palmer et al., 1989). False pregnancy in bitches is accompanied by specific behavior – the animals are restless, engage in nesting behavior and treat toys as they would their newborn offspring. Enlargement of the mammary glands, secretion and leakage of milk and increased appetite are all observed. Retained milk may lead to inflammation of the mammary gland, followed by neoplastic lesions.

**Diagnosis and treatment of hyperprolactinemia**

Diagnosing hyperprolactinemia is not a simple task. Not all cases of this condition are accompanied by characteristic symptoms such as enlarged mammary glands. Humans exhibit nonspecific symptoms which include anxiety, irritability, depression, fatigue, emotional lability, headaches. Detection rate of the relationship between infertility and the LUF syndrome oscillates between 5% and 57% – that disparity can be explained by the wide range of methods used to detect hyperprolactinemia. Diagnosis is rendered more difficult by the fact that prolactin isoforms differ both in structure and molecular weight; this means there is no single diagnostic system which allows detecting all prolactin isoforms in the body at the same time, making up a "total" concentration of this hormone measured all at once. A good example is the isoform known as macro-prolactin, BB-PRL, which is a hormone molecule complexed with immunoglobulin G. This results in large differences in test results and incorrect diagnosis. Due to existence of prolactin isoforms, immunometric tests such as ILMA

(immunoluminometric method), IRMA (radio-immunometric method) and ELISA (immunoenzymatic method) used for determining concentration of prolactin in laboratories often give false negative results. Substances affecting intensity of prolactin secretion are used in the treatment of hyperprolactinemia (Liukkonen et al., 1984).

Modulation of PRL levels with pharmaceuticals is mediated via their reaction with dopamine receptors. Both antagonists and D2 receptor agonists can be found among drugs used to modulate PRL levels. The first group includes domperidone, metoclopramide, and sulpiride, and the latter – cabergoline, bromocriptine and quinagolid. Substances known as antagonists of D2 receptors block the dopamine receptors, resulting in increase in PRL concentration (Kałużny and Bolanowski, 2005). The quantity of milk produced by mammary glands of mares depends on the ovarian hormones (Nagy and Neill, 1994). The increase in prolactin level results in increased ovarian susceptibility to the effects of FSH and LH, as it contributes to stimulation of gonadotropic receptor expression. In case of problems with lactogenesis in women, a successfully used drug is metoclopramide. It was attempted to use this substance to experimentally increase concentration of PRL in mares – lack of positive result of the attempt is due to a significantly shorter period of metoclopramide activity compared with sulpiride (Johnson and Becker, 1987).

Hyperprolactinemia in mares, women, bitches and other mammalian species can be successfully controlled with the aid of substances that are D2 receptor agonists. Administration of these drugs contributes to a decrease in PRL concentration. Cabergoline (cabergolinum) is an organic chemical compound, a derivative of the ergot alkaloids. Cabergoline is an ergoline derivative with potent and long-acting dopaminergic effects. The drug directly stimulates $D_2$ dopamine receptors of the anterior lobe of the pituitary, which inhibits the secretion of prolactin. At higher than therapeutic concentrations of cabergoline, the drug acts on the central nervous system. Cabergoline is highly selective – it does not affect the production and secretion of other pituitary hormones and cortisol. Cabergoline also has hypotensive effects. The drug is used to treat pituitary adenoma (prolactinoma), idiopathic hyperprolactinemia, and an empty sella syndrome associated with hyperprolactinemia, and finally in order to disrupt or inhibit lactation. The substance demonstrates beneficial effects in conditions associated with excessive secretion of prolactin, such as menstrual disorders (none, sparse or irregular menses), anovulation, galactorrhea. In contrast to bromocriptine, it has no side effects (Johnson and Becker, 1987).

Bromocriptine is a semisynthetic derivative of ergocriptine. The drug acts by stimulating D2 dopaminergic receptors in the hypothalamus. The substance acts on the pituitary cells through production of dopamine (an inhibitory factor). It inhibits the production and secretion of prolactin from the anterior pituitary and in acromegaly reduces the secretion of growth hormone, but it does not impact the secretion of other pituitary hormones (Molik et al., 2015). It also inhibits the growth of pituitary adenomas (prolactinomas), and in hyperprolactinemia reduces the concentration of prolactin. It has also proven antidepressant effects, and in Parkinson's disease acts on dopamine receptors in the striatum and limbic system, reducing tremors and akinesia. It is absorbed well from the gastrointestinal tract (1–3 h). In 96%, it binds to plasma

proteins, and is almost entirely eliminated with the bile and feces (partly in the form of metabolites), with just a several percent eliminated with urine.

Bromocriptine administration to women with hyperprolactinemia stimulates ovulation and a similar effect has been observed in mares treated with this drug during lactation anoestrus. Bromocriptine causes a marked decrease in prolactin concentration only in situations when the level of this hormone in the blood is high – there were no statistically significant changes in the PRL concentration after administration of bromocriptine to animals whose hormone levels had been low before the drug was used (Johnson and Becker, 1987).

Quinagolid is a synthetic, selective dopamine D2 receptor agonist with prolonged action, that is neither an ergot nor an ergoline derivative. It is the active substance of a drug known under trade name Norprolac that is used in the treatment of hyperprolactinemia of idiopathic origin, as well as that caused by micro- or macro-adenomas of the pituitary. The drug exerts a strong inhibitory effect on secretion of prolactin, but does not weaken the secretion of other pituitary hormones. After oral administration, it is rapidly absorbed from the gastrointestinal tract, metabolized in the liver and in more than 95% excreted as metabolites. Clinical response in the form of substantial reduction in prolactin concentration occurs within 2 h after administration, reaches a peak within 4–6 h, and is maintained for about 24 hours (Karasek et al., 2006). Side effects after administration of the drug include nausea, vomiting, headaches, dizziness and fatigue. In addition, these might be accompanied by loss of appetite, abdominal pain, constipation or diarrhea, insomnia, edema, flushing, nasal congestion, orthostatic hypotension and fainting spells. In the event of excessive dosage, patients exhibit drowsiness and have difficulties concentrating. In individual cases, severe psychotic symptoms have been observed (Lech, 2005). Substances that are antagonists of dopamine receptors have an inhibitory effect on the action of quinagolid. Therefore, any use together with agonists or antagonists of the 5-HT1A receptors and antagonists of the 5-HT2 receptors should take place under medical supervision.

The key goal of animal farmers is to achieve the highest possible profit while minimizing the costs entailed in livestock or dairy production. In the process of reducing economic losses, an important role is played by combating animal diseases. Research leading to deeper understanding of physiology of dysfunctions resulting in impaired fertility is crucial in development of the most effective methods of treatment.

**Conclusions**

The present paper was aimed at gathering information available on hyperprolactinemia, a hormonal dysfunction that is difficult to treat and results in impaired reproductive cycles. Difficulties in diagnosis of the said dysfunction and the sometimes ineffective treatment extend the production cycle duration. Occurrence of hyperprolactinemia is associated with an increase in animal maintenance costs. Data collected so far is not sufficient to completely eliminate this hormonal dysfunction and its consequences; further research is needed to develop increasingly sophisticated methods of treatment of hyperprolactinemia in both animals and humans.

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