SUMMARY

The human body as well as the animal body is similar to a planet invaded by alien bodies. Therefore, bacteria represent the body's "infantry" responsible for conducting a constant dialogue with the immune system.

The immune system requires an acquisition process which is accomplished by developing a network aimed at establishing the connexion among bacteria as well as a connexion between bacteria, the body and the immune system, respectively. They teach the immune system how to destroy invaders. The immune system uses its "soldiers", the neutrophils (the primary defence system), to attack and destroy "enemy" ground.

Microbes form ecosystems both inside and outside our bodies in order to allow our bodies to live and be healthy.

A good understanding of the body's capacity to protect itself against "invaders" is therefore the result of a sound evaluation of the functioning of a body's humoral immune system.

In this context, the research topic of the doctoral thesis is focused on the circadian biorhythm as well as on the seasonal rhythm of the most important factors characterising the immune system specific to cattle.

The researches were conducted using a total number of 132 brown Swiss cattle, aged 3 to 10. Within 365 days, the clinical and haematological investigations were carried out throughout all the seasons, usually at mid-season. The season specific researches on the evolution of the cellular and humoral elements of blood (haematological) were carried out on a group of 15 dairy cattle, their blood samples being taken at the beginning of the season, towards the end of the first month of that particular season. The season specific and the annual determinations were carried out on blood samples taken at 6 am, 12 am, 6 pm, and 12 pm, respecting day/night cycle. The same haematological investigation was carried out on a group of 15 clinically healthy cattle, a group of 15 cattle suffering from various genital disorders, and on a group of 33 cattle suffering from digestive,

respiratory, genitourinary and musculocutaneous disorders, in order to test the efficiency and efficacy of the therapy. The determinations were carried out on blood samples taken at 8 am.

The analysis and synthesis of our own researches on the circadian evolution of the primary and secondary cellular factors of immunity are relevant for the evaluation of the body's physiological state as far as its behaviour within and reaction to its environment are concerned.

Therefore, one of the main findings of the research was that the body's **global leukocyte** reaction implies a growth in the number of leukocytes starting with 12 noon and maximum values around 12 midnight, followed by a decrease in their number until morning when they register the lowest level. As soon as the bodies start functioning, the number of these factors starts increasing to the point where they play an essential part in the unspecific and specific reaction that the body develops in order to protect itself against internal and external aggressors ($p \leq 0.05$).

There were also daily variations in the number of neutrophil, eosinophil and basophil granulocytes. The **neutrophils** registered a high level during daytime, especially around 12 noon and a low level at night and early in the morning ($p \leq 0.01$). The **eosinophils** registered a high level in the evening and at night and a low level in the morning, the moment after which they registered an increasing level ($p \leq 0.001$ şi $p \leq 0.05$). The **basophils** registered a high level in the evening and at night and a low level in the morning, the moment after which they registered an increasing level ($p \leq 0.05$). Variations in the number of **granulocytes** indicates their physiological involvement in the natural and acquired immunity of the body.

The **monocytes,** the main components of the reflex immune system, registered a high level in the morning, especially around 12 noon, and a low level in the evening and at night, the moment after which their level started growing only to reach a maximum value at noon ($p \leq 0.05$).

The evolution of **lymphocytes** emphasised the fact that these blood cells register a high level in the morning, an average level at night, the lowest level being registered around 12 noon, the moment after which they register an increasing level until morning ($p \leq 0.001$ şi $p \leq 0.01$). As far as their **sizes** are concerned, the most frequent are the *medium lymphocytes*, followed by the *small lymphocytes*, the least numerous being the *large lymphocytes.* As far as the **intracytoplasmic granulations** are concerned, the most predominant are the non-granulated lymphocytes. The behaviour of lymphocytes, the cells of specific (adaptive) immunity illustrate the physiological mechanism of the body's specific immunity, the part that lymphocytes play in every stage of a body's life.

Together with these cellular components specific to the body's defence system, one can also mention the elements of the red series and the trombocytes. The data resulting from our own research emphasise that the **erythrocytes** register a high level at night and from early in the morning till noon and a low level in the evening ($p \leq 0.05$ and $p \leq 0.001$, respectively).

The level of hemoglobin is high in the morning, lower in the evening and registers the lowest level at night, especially around 12 midnight ($p \leq 0.001$ and $p \leq 0.05$ and $p \leq 0.05$, respectively). The **hematocrit** registers a high level in the morning and at night and a lower level at noon and in the evening ($p \leq 0.001$). The **erythrocytes indices** (MCH and MCHC) register a high level in the morning and at noon (($p \leq 0.05$ for MCV and MCH) as well as from early in the morning until late in the evening ($p \leq 0.001$ for MCHC) and a low level at night.

As far as leukocytes were concerned, the season specific biorhythm of the cellular reaction of immunity was illustrated as follows: the level of leucocythaemia was high in spring and summer, the lowest level being registered in autumn whereas the greatest amount of leukocytes was registered in the evening and at night throughout all the seasons ($p \leq 0.05$, $p \leq 0.01$, $p \leq 0.001$); the neutrophils and the monocytes registered high levels in summer and autumn and lower levels in winter and spring. The level of neutrophils was high at noon and in the evening whereas the level of monocytes was high in the morning and at noon ($p \leq 0.05$, $p \leq 0.01$). As far as basophils were concerned, they registered a high level in spring and summer and a low level in winter and autumn, the highest level being registered around 6 pm and 12 midnight. Lymphocytes registered their highest level in winter and spring. Throughout the seasons, the highest levels were registered at 6 am and 12 midnight whereas the lowest levels, at 12 noon. The red cells did not show significant variations.

Circadian variations of the globulins in blood throughout 365 days were illustrated as follows: the γ serum globulins registered a high level at 6 am, 6 pm and 12 midnight and a lower level at 12 noon ($p \leq 0.05$, $p \leq 0.01$, $p \leq 0.001$); the beta serum globulins registered a high level at noon and in the evening and a lower level at night ($p \leq 0.001$) and in the morning (6 o'clock); the alpha-1 serum globulins registered a high level at night ($p \leq 0.001$) and a slightly lower level in the morning, at noon and at night; the alpha-2 globulins registered a low level at night (12 midnight) ($p \leq 0.05$) and a slightly higher level at 12 noon and 6 pm.

The season specific biorhythm of serum globulins and serum albumins indicated the following: the γ serum globulins registered a high level in winter and a low lever in autumn and, as far as the moment of the day is concerned, in winter and autumn they registered their highest level at

12 midnight and in spring and autumn, at 6 am ($p \leq 0.01$, $p \leq 0.05$); the beta serum globulins registered a high level in winter and a gradually decreasing level in spring, autumn and summer, the highest levels being registered at 12 noon, in summer and autumn and at 6 pm in spring. The lowest levels were registered at six o'clock in the morning for all seasons ($p \leq 0.05$, $p \leq 0.01$); the alpha-1 serum globulins registered a high level in autumn, followed by spring, summer and autumn, at 6 am in winter, 6 pm in spring and 12 midnight in autumn ($p \leq 0.05$, $p \leq 0.01$); the alpha-2 serum globulins registered the highest level in winter, followed by autumn, spring and summer, at 6 pm in winter, spring and autumn and at 6 am in summer ($p \leq 0.01$). The serum albumins registered a high level in autumn, followed by summer, spring and winter, at 6 am in winter and autumn and at 12 noon in spring and summer ($p \leq 0.05$).

The determination of the **interferon** emphasised the presence of the interferon receptor IFNγ in monomeric and dimeric form in the case of healthy animals and in monomeric, dimeric and tetrameric form in the case of sick animals, the latter presenting a higher level of interferon.

The results of the researches on the body's physiological balance in relation to the biorhythm of the immune profile emphasised that glucose registered an average level of 57.50 mg/dl, triglycerides, 31.85 mg/dl, cholesterol, 134.30 mg/dl, dairy protein, 20.70 mg/dl, and beta-hydroxybutyrate, 0.29 mg/dl. The average level of the mineral profile was distributed as follows: calcium – 10.12 mg/dl, magnesium – 2.08 mg/dl, and phosphorus – 3.53 mg/dl. The average level of the hepatorenal indices was distributed as follows: urea nitrogen – 33.21 mg/dl, creatinine – 1.61 mg/dl, uric acid – 2.13 mg/dl, GPT (Glutamate-Pyruvate Transaminase***)*** – 30.04 iu/l, GOT – 107.2 iu/l, GGT – 28.36 iu/l, ALP – 124.62 iu/l and amylose – 13.52 iu/l.

The efficiency of medication related to the circadian biorhythm emphasised the fact that the highest percentage of cured animals after a 3-day treatment was registered in the case of animals that were treated in the morning (36.3%), followed by those treated in the evening (23.6%) and by those treated twice a day, in the morning and in the evening (12.5%).

The recovery of the animals after a 5-day treatment indicated the following percentages: 36.3% in the case of animals treated in the morning, 30.7%, in the evening, and 50%, in the case of animals treated twice a day (in the morning and in the evening).