10

Acute Phase Proteins in Dairy Cows and Sows During the Periparturient Period

Gabriel Kováč, Csilla Tóthová,
Oskar Nagy and Herbert Seidel
University of Veterinary Medicine and Pharmacy in Košice
Slovak Republic

1. Introduction

Acute phase proteins have been used as biomarkers of diseases for decades in human medicine, but have been relatively under-utilised in the veterinary medicine. Over recent years, significant progress has been made in studies on acute phase response in farm animal medicine, including the detection, measurement and application of acute phase proteins as biomarkers of diseases in both cattle and pigs. Acute phase proteins are blood proteins primarily synthesized by hepatocytes as part of the acute phase response. The acute phase response is a complex systemic early-defense system activated by impaired homeostasis, trauma, tissue injury, infection, inflammation, stress or neoplasia (Cray et al., 2009). This response leads to a range of metabolic activities and alterations in a wide variety of biochemical processes. One of the most important metabolic changes during the acute phase response is the strongly increased or decreased production and secretion of some plasma proteins from the liver, the acute phase proteins (Murata et al., 2004). Although non-specific, the acute phase response serves as a core of the innate immune reactions involving physical and molecular barriers and responses with the goal to prevent infection, clear potential pathogens, and contribute to the resolution and healing processes (Petersen et al., 2004).

Much of the recent attention on the assessment of acute phase proteins in farm animals has resulted not only from the advances described above, but also because they have been recognized as valuable markers of diseases. As indicators of inflammation, the assays of acute phase proteins provide valuable additional information to more traditional haematological and biochemical investigations (Skinner et al., 1991; Eckersall, 2000). Application of acute phase protein analyses in disease investigations also in farm animals has shown that it has a major diagnostic contribution to make in the evaluation of various inflammatory, as well as non-inflammatory diseases (Gruys et al., 2005). In the clinical field, acute phase proteins may serve as non-specific indicators of health status and surveillance of animals at the herd level. In the last decade, emphasis has been laid also on the application of blood test for acute phase reactants to monitor animals suffering from specified classes of diseases. However, the behavior of acute phase proteins in some disease, as well as physiological conditions, e.g. during the reproduction cycle of cows and sows,

particularly around the parturition, still remain to be uncovered. Moreover, the pathophysiology of the changes in the concentrations of acute phase proteins in relation to some metabolic and biochemical reactions, as well as the relationships between immune functions and metabolic adaptations during some disease and physiological conditions are less well documented. These conditions involve e.g. changes in the concentrations of acute phase proteins in relation to altered metabolism, especially energetic metabolism in dairy cows around the parturition.

2. Acute phase proteins in farm animals

Animals undergoing external or internal challenge to their state of health manifest a vigorous response including activation of both the innate and acquired immune systems. The natural immunity is phylogenetic older, and is characterized by uniform nature to any intruder, and by immediate response (Janeway et al., 2001). The mechanisms of natural immunity defend an organism since the very first second of a danger. The defence mechanisms of innate immunity are numerous; the acute phase response belongs to those of the most important (Murata et al., 2004). It is designed to hold the infection in check until the adaptive, highly specialized immune response is initiated, which is followed by repairing processes terminating the episode of inflammation bringing the organism back to its physiological state (Baumann & Gauldie, 1994).

The varied reactions of the host to disturbances in its homeostasis caused by infection, tissue injury, trauma or surgery, neoplastic growth or immunological disorders are collectively known as the acute phase response, and encompass a wide range of pathophysiological responses (Johnson, 1997; Gruys et al., 1999) (Fig. 1). At the site of invasion by microorganisms and at the place of tissue injury, a number of responses of the tissue itself are initiated (Koj, 1996; Cray et al., 2009). Pro-inflammatory cytokines are released, subsequently, to activation of the immune and the vascular systems (Bellomo, 1992; Gruys et al., 2005). Another systemic response to injury is an increase or decrease in the production of a number of plasma proteins produced by the liver, which are known as acute phase proteins (Whicher & Westacott, 1992). These biomarkers are highly sensitive indicators of inflammation, but there are major differences among species in their acute phase response (Pyörälä, 2000). As described by Eckersall & Bell (2010), haptoglobin and serum amyloid A are the diagnostically most valuable acute phase proteins in cattle. In the pig, C-reactive protein, haptoglobin, and α_1-acid glycoprotein were identified as the major acute phase proteins (Du Clos, 2004).

Acute phase proteins might be applied as non-specific markers of clinical infections, and for prognostic purposes (Lauritzen et al., 2003). Measurement of acute phase proteins can detect or confirm the presence of infection or pathological lesion, but a major role for these analytes could be in the monitoring of the health status of animals in the production. Acute phase proteins can detect the presence of sub-clinical diseases, which are the cause of reduced growth rate and lost production (Eckersall, 2000). In the pig production system, health status is usually accepted that individuals are infectious agents-free. However, the pigs might be frequently infected leading to poor health despite high health declarations that may cause suboptimal growth and decreased welfare (Toussaint et al., 2000). Acute phase protein testing offers a tool for assessing health estimation based on the extent of inflammation and tissue damage (Petersen et al., 2004).

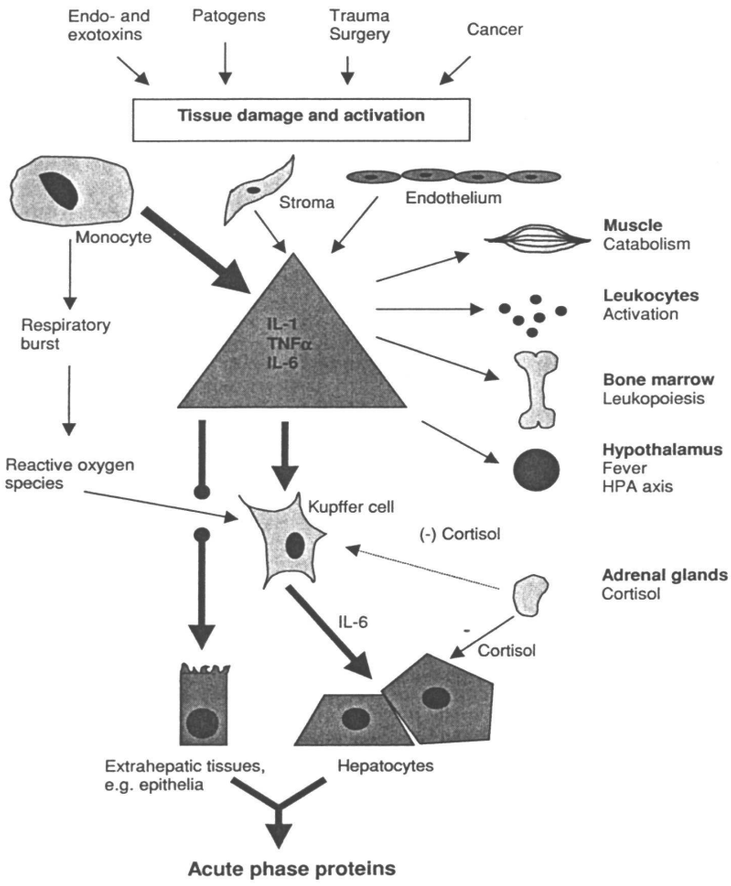


Fig. 1. The acute phase response (Jacobsen, 2003)

3. Acute phase proteins and the period after parturition in dairy cows

The period after parturition is the most critical period in dairy cows regarding health status and production. Factors such as pregnancy, parturition, blood calcium concentrations, initiation of lactation and feed intake all affect the ability of the cow's immune system to efficiently combat infections. The periparturient period is the time where complex physiological changes occur simultaneously, having a significant effect on the animal's health (Cai et al., 1994; Lippolis, 2008). Parturition, changes in homeostasis, metabolic and physiological challenges occuring in this stressful period, as well as other external and internal harmful stimuli may contribute to the activation of host immune system and inflammatory responses, including the initiation of the production of acute phase proteins.

Acute phase proteins have various activities by which contribute to germs destruction, to reduce tissue damage and help its regeneration (Pyörälä, 2000). Major bovine acute phase proteins, haptoglobin and serum amyloid A, play an important role also in the reproductive processes, they intensify the phagocytosis process against the pathogens introduced into the uterus, and help by the reconstruction of the endometrium (Regassa & Noakes, 1999; Krakowski & Zdzisińska, 2007).

Moreover, the transition of pregnancy to lactation, with the concomitant negative energy balance during early lactation, requires substantial adaptation of the cow, including

metabolic and physiological adaptations, and is accompanied by changes in whole metabolism (Hachenberg et al., 2007; Leroy et al., 2008). It has been described in human medicine that physiological reactions around parturition, as well as metabolic changes are known to trigger several key events that can initiate and promote uncontrolled systemic inflammation (Gatzka et al., 2002; Sordillo et al., 2009). Yaqoob & Calder (2007) reported that in humans, altered lipid metabolism, increased circulating concentrations of non-esterified fatty acids and oxidative stress are factors that significantly contribute to both systemic inflammation and development of inflammatory-dependent diseases. Dairy cows undergo similar metabolic adaptations and changes in homeostasis after parturition. However, the pathophysiology of the aforementioned metabolic events and changes in immune functions are less clear.

4. Acute phase proteins in relation to the reproduction cycle of sows

Reproductive state and parity are important factors influencing most of the biochemical parameters of sows (Reese et al., 1984). In general, the time around parturition is the most challenging period of the reproduction cycle. Nutritional and metabolic stress around parturition is an increasingly important phenomenon because during this period the physiological balance of the animal is challenged. These phenomena and underlying mechanisms can be reflected in several endocrinological, immunological and biochemical parameters. Moreover, animals may react to disturbances in their homeostasis not only with systemic reactions, but also with increased production of acute phase proteins (Marnell et al., 2005).

In sows, there are very scarce data about the changes in the concentrations of acute phase proteins in connection to the reproduction cycle. It has been described in humans that the concentrations of most of the acute phase proteins do not change during pregnancy, but increase at parturition (Berkova et al., 2001). It is important to realize that physiologically, acute phase proteins may react at parturition also in animals (Alsemgeest et al., 1993). The time around parturition and its metabolic challenges constitute a potentially stressful period, if stress is defined as the impact of external and internal stimuli that challenge homeostasis (Moberg, 2000). Animals react to disturbances in their homeostasis with a set of physiological changes and systemic reactions like fever, alterations of appetite, and decreases in serum concentrations of iron and zinc. The most striking phenomenon, however, is the changing concentration in a number of serum proteins, particularly acute phase proteins (Petersen et al., 2004).

The stress due to prefarrowing dislocation and farrowing might activate subclinically present chronic urogenital infections, resulting in postparturient diseases of sows (Glock & Bilkei, 2005). Urinary tract infection, postparturient swine urogenital diseases, chronic endometritis, and mastitis-metritis-agalactia syndrome are the most important diseases affecting the sows in the early postparturient period (Thornton et al., 1998; Waller et al., 2002). These important disorders of the sows may cause increased values of acute phase proteins and may contribute to lower number of piglets in litter, inadequate lactation, even to sow mortality (Mirko & Bilkei, 2004). However, the influence of reproduction stage, predominantly parturition on the concentrations of acute phase proteins in sows is less well documented.

Therefore, here we propose a two-phases study. The first objective was the assessment of concentrations of some selected acute phase proteins and variables of energetic metabolism in

dairy cows after parturition, as well as at the evaluation of the relationships between the activated acute phase response, characterized by higher concentrations of acute phase proteins, and between altered energetic metabolism shortly after calving. The second objective of this study was to evaluate the concentrations of selected acute phase proteins – haptoglobin and C-reactive protein in blood serum of sows during different stages of reproduction cycle, including the period before and after farrowing, as well as after weaning.

5. Material and methods

5.1 Relationships between acute phase proteins and altered energetic metabolism in dairy cows after calving

5.1.1 Animals and clinical examination

The evaluation of the relationships between the concentrations of acute phase proteins and some variables of energetic metabolism shortly after parturition was performed in 195 dairy cows of a Slovak spotted breed and its crossbreeds on a farm of high yielding dairy cows. The monitored cows were in a period of 1 – 2 weeks after parturition. The animals were housed loosely, and fed twice a day individual feeding rations according to the phase of lactation with free access to water. Before sample collection, the cows were examined clinically using standard clinical examination procedures (Jackson & Cockcroft, 2002). The evaluated cows showed no health disorders during the observation.

5.1.2 Laboratory analyses

The laboratory analyses of evaluated parameters were performed in blood samples. Blood for the investigations was taken by direct puncture of *v. jugularis*. Blood samples were collected into plastic serum tubes with clot activator and gel without anticoagulant. The separated serum was stored at -20 °C until analyzed. Blood serum was analyzed for selected acute phase proteins – haptoglobin (Hp, mg/ml) and serum amyloid A (SAA, μg/ml), and variables of energetic metabolism – glucose (Glu, mmol/l), total cholesterol (TCH, mmol/l), total lipids (TL, g/l), triglycerides (TG, mmol/l), non-esterified fatty acids (NEFA, mmol/l), and β-hydroxybutyrate (BHB, mmol/l).

Haptoglobin was assessed using commercial colorimetric kits (Tridelta Development, Maynooth, Ireland) in microplates, based on Hp-haemoglobin binding and preservation of the peroxidase activity of the bound haemoglobin at low pH. Serum amyloid A was analyzed by method of sandwich enzyme linked immunosorbent assay using commercial ELISA kits (Tridelta Development, Maynooth, Ireland). The reading of absorbancies and the consecutive calculation of final concentrations of both acute phase proteins were performed on automatic microplate reader Opsys MR (Dynex Technologies, Chantilly, USA). The concentrations of Glu, TCH, TG, and BHB were determined using commercial diagnostic kits (Randox) on automatic biochemical analyser ALIZE (Lisabio, Pouilly en Auxois, France). Total lipids were analyzed using commercial diagnostic kits (Ecomed, Zilina, Slovak Republic) by spectrophotometric method. The concentrations of NEFA were assessed according to Curtius (1974) by spectrophotometric method.

5.1.3 Study groups

The obtained results from evaluated cows were divided into two groups according to the measured concentrations of NEFA: Group A (n = 108) – cows with serum concentrations of NEFA below 0.35 mmol/l; Group B (n = 87) – cows with serum concentrations of NEFA above 0.35 mmol/l.

5.1.4 Statistical analyses

Statistical analyses of experimental results were performed by assessment of average values (x) and standard deviations (SD) in each group of cows. The significance of the differences in the obtained results (P) of corresponding variables between monitored groups of animals was evaluated by Mann-Whitney nonparametric test. The relationships between the concentrations of evaluated variables in the monitored cows were calculated by linear regression and Spearman (R) correlations coefficient, including significance of the correlation. Statistical analyses were done in the programme GraphPad Prism V5.02 (GraphPad Software Inc, San Diego, USA).

5.2 The concentrations of selected acute phase proteins during the reproduction cycle of sows

5.2.1 Animals and sample collection

The evaluation of the influence of different stages of the reproduction cycle on the concentrations of selected acute phase proteins included 24 sows, which were crossbreeds of large white and landrace after 1–5 farrowings. The animals were fed complete feedstuff according to corresponding stages of reproduction cycle twice a day, and they had free access to drinking water. Before each sample collection, the animals were clinically examined by standard clinical examination procedures (Jackson & Cockcroft, 2002).

The monitored sows were divided into 4 groups according to different stages of reproduction cycle at the beginning of the evaluation: Group I (n = 6) – sows 4 weeks before farrowing, Group II (n = 6) – sows 1 week before farrowing, Group III (n = 6) – sows 1 week after farrowing, Group IV (n = 6) – sows 1 week after weaning.

Blood for the investigations was collected by direct puncture of *v. cava cranialis* into plastic serum tubes with clot activator and gel without anticoagulant. Blood samples were taken in each group of sows four times at intervals of two weeks (Table 1).

Groups of sows	Sample collections			
	1st	**2nd**	**3rd**	**4th**
I	4 weeks *a.p.*	2 weeks *a.p.*	1–2 days *p.p.*	2 weeks *p.p.*
II	1 week *a.p.*	1 week *p.p.*	3 weeks *p.p.*	1 week *p.* wean.
III	1 week *p.p.*	3 weeks *p.p.*	1 week *p.*wean.	3 weeks *p.*wean.
IV	1 week *p.*wean.	3 weeks *p.*wean.	5 weeks *p.*wean.	7 weeks *p.*wean.

a.p. – ante partum, p.p. – post partum, p. wean. – post weaning

Table 1. Time-table of blood sample collections within the evaluated groups of sows

In the first part of the study, we evaluated the dynamics of changes in the concentrations of measured acute phase proteins during the reproduction cycle in the mentioned groups of sows. In the second part of the study, we summarised the individual values of acute phase proteins from these groups of sows according to four selected periods of reproduction cycle – 4 weeks *ante partum*, 1 week *ante partum*, 1 week *post partum* and 1 week *post* weaning.

5.2.2 Laboratory analyses

Venous blood samples were centrifuged at 3.000 g for 30 minutes. Serum was separated and stored at -18 ˚C until laboratory analyses could be performed. Blood serum was analyzed for selected acute phase proteins – haptoglobin (Hp, mg/ml), and C-reactive protein (CRP, ng/ml).

Haptoglobin was assessed using commercial colorimetric kits (Tridelta Development, Maynooth, Ireland) in microplates. Blood serum samples were initially diluted 1:5. C-reactive protein was analyzed by method of sandwich enzyme linked immunosorbent assay using commercial ELISA kits (Tridelta Development, Maynooth, Ireland). Serum samples for the determination of CRP were diluted 1:500 prior to assay. The optical densities were read on the automatic microplate reader Opsys MR (Dynex Technologies, Chantilly, USA) at 630 nm for Hp, and at 450 nm using 630 nm as reference for CRP.

5.2.3 Statistical analyses

Statistical evaluation of the obtained results was performed by assessment of means (x) and standard deviations (SD) in each monitored group of sows according to the sample collection. The significance of the differences in measured values (P) of the investigated variables in relation to the corresponding monitored periods of reproduction was evaluated by one way analysis of variance (ANOVA). The significance of differences in measured values between the sample collections in the groups was evaluated by Student's paired test (the 1st part of the study), and the significance of differences in the obtained concentrations between selected periods of reproduction cycle was evaluated by Student's unpaired test (the 2nd part of the study).

6. Results

6.1 Relationships between acute phase proteins and altered energetic metabolism in dairy cows after calving

The results of the concentrations of selected acute phase proteins, and variables of energetic metabolism characterised by average values (x) and standard deviations (SD), as well as the evaluation of the significance of differences in the obtained results (P) between two groups of cows are given in Table 2, and on Fig. 2 and 3. The analyses of relationships between monitored variables in cows are summarised in Table 3 and are shown on Fig. 4 - 7.

Soluble factors	**Group of cows**		**P**
	A (n = 108)	**B** (n = 87)	
Hp (mg/ml)	0.067 ± 0.113	0.607 ± 0.610	< 0.001
SAA (µg/ml)	30.77 ± 20.95	93.94 ± 43.64	< 0.001
Glu (mmol/l)	4.19 ± 0.57	3.95 ± 0.44	< 0.001
TCH (mmol/l)	3.25 ± 1.11	3.05 ± 1.12	n. s.
TL (g/l)	3.48 ± 1.44	3.43 ± 1.31	n. s.
TG (mmol/l)	0.14 ± 0.11	0.12 ± 0.09	n. s.
NEFA (mmol/l)	0.21 ± 0.09	0.65 ± 0.25	< 0.001
BHB (mmol/l)	0.46 ± 0.26	0.65 ± 0.35	< 0.001

Group A – cows with serum concentrations of NEFA below 0.35 mmol/l; Group B – cows with serum concentrations of NEFA above 0.35 mmol/l

P – significance of the differences in the obtained results between the groups of cows, n. s. – non significant

Table 2. Comparison of the concentrations of Hp, SAA and selected variables of energetic metabolism in two groups of dairy cows (x ± SD)

In cows with serum concentrations of NEFA above 0.35 mmol/l we found significantly higher mean value of haptoglobin than in cows with NEFA concentrations below 0.35 mmol/l ($P < 0.001$, Table 2). It is shown on Fig. 2 that while in cows with serum NEFA concentrations below 0.35 mmol/l (Group A) the median Hp concentration was 0.029 mg/ml and the individual values ranged from 0.001 to 0.697 mg/ml, in cows with NEFA values above 0.35 mmol/l (Group B) we recorded higher median Hp concentration (0.470 mg/ml), as well as markedly wider range of individual values with minimum concentration of 0.006 mg/ml and maximum value of 2.540 mg/ml. By more detailed analysis of individual Hp concentrations we found that while in Group A 50 % of measured values ranged from 0.010 mg/ml to 0.067 mg/ml, in Group B this range was from 0.162 mg/ml to 0.834 mg/ml.

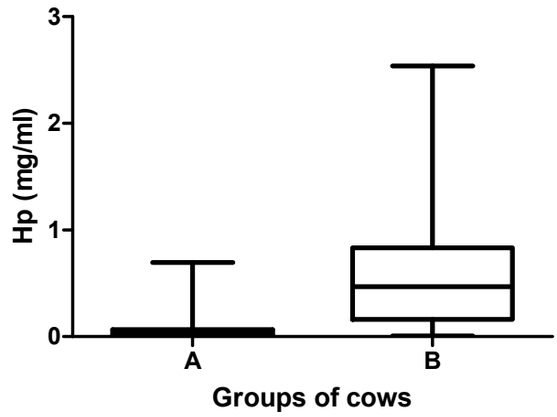


Fig. 2. The concentrations of Hp in serum from cows with NEFA concentrations below 0.35 mmol/l (Group A) and above 0.35 mmol/l (Group B). The plots show the median (line within box), 25th and 75th percentiles (box)), minimum and maximum values (whiskers)

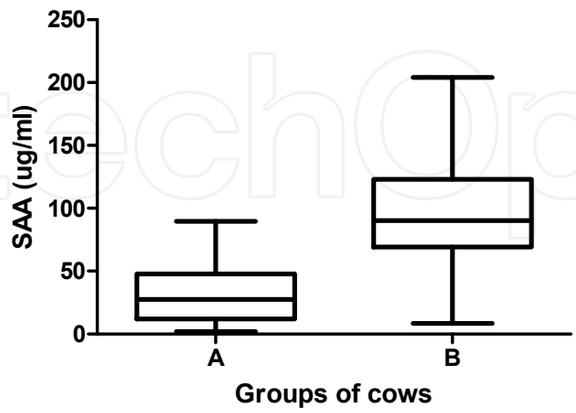


Fig. 3. The concentrations of SAA in serum from cows with NEFA concentrations below 0.35 mmol/l (Group A) and above 0.35 mmol/l (Group B). The plots show the median (line within box), 25th and 75th percentiles (box), minimum and maximum values (whiskers)

In cows with concentrations of NEFA above 0.35 mmol/l, significantly higher mean serum concentration was found also for SAA ($P < 0.001$). The median SAA concentration in cows from Group A was 27.70 μg/ml, and the individual values ranged from 1.95 μg/ml to 89.78 μg/ml (Fig. 3). The median SAA concentration in cows from Group B was higher (90.30 μg/ml), and the measured concentrations showed wider range of individual values (from 8.38 μg/ml to 204.00 μg/ml).

Trend of significantly higher values in cows with NEFA concentrations above 0.35 mmol/l was found also in the serum concentrations of BHB ($P < 0.001$). On the other hand, cows with higher values of NEFA showed significantly lower mean concentration of glucose ($P < 0.001$). In mean concentrations of total cholesterol, total lipids, and triglycerides we observed no significant differences between two groups of cows.

By the assessment of correlations we recorded a significant positive correlation between the concentrations of both measured acute phase proteins – Hp and SAA, and the values of NEFA ($R = 0.716$, $P < 0.001$; $R = 0.710$, $P < 0.001$, respectively), as well as the values of BHB ($R = 0.291$, $P < 0.001$; $R = 0.300$, $P < 0.001$, respectively) (Figs. 4 - 7).

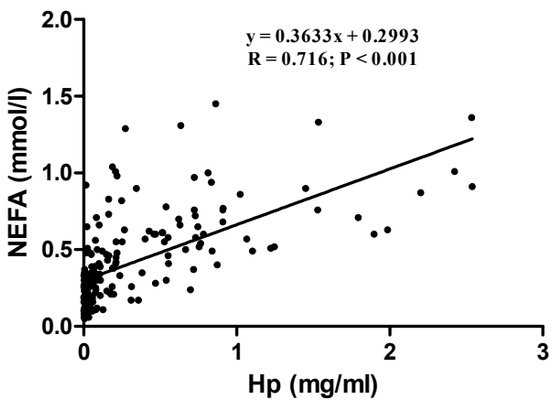


Fig. 4. Correlation and regression analysis between Hp and NEFA concentrations

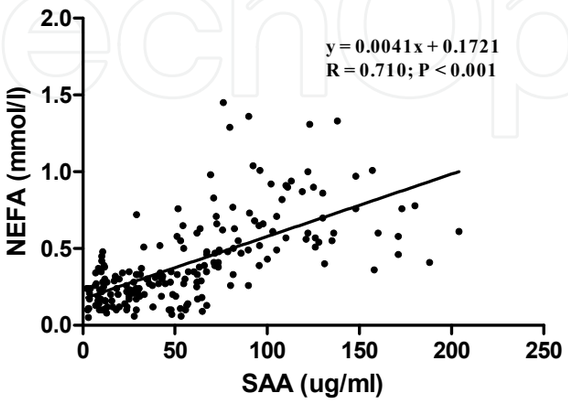


Fig. 5. Correlation and regression analysis between SAA and NEFA concentrations

Significant negative correlations was found between the concentrations of both acute phase proteins and the values of glucose (R = -0.247, P < 0.001; R = -0.249, P < 0.001, respectively), as well as the concentrations of total cholesterol (R = -0.181, P < 0.05; R = -0.241, P < 0.001, respectively). Moreover, the concentrations of Hp in cows shortly after parturition significantly positively correlated with the values of SAA (R = 0.647, P < 0.001). Significant correlations we observed also between some variables of energetic metabolism, which are listed in Table 3.

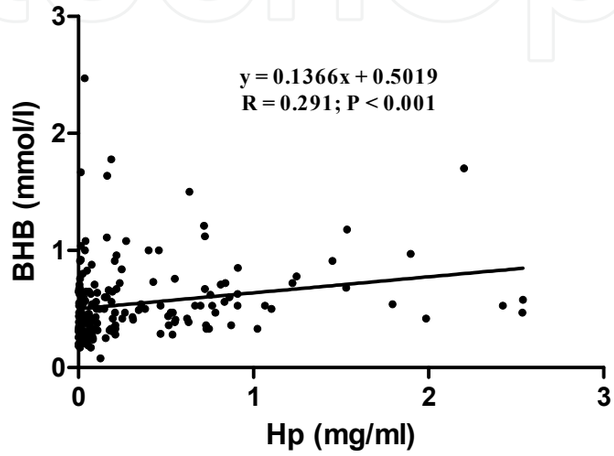


Fig. 6. Correlation and regression analysis between Hp and BHB concentrations

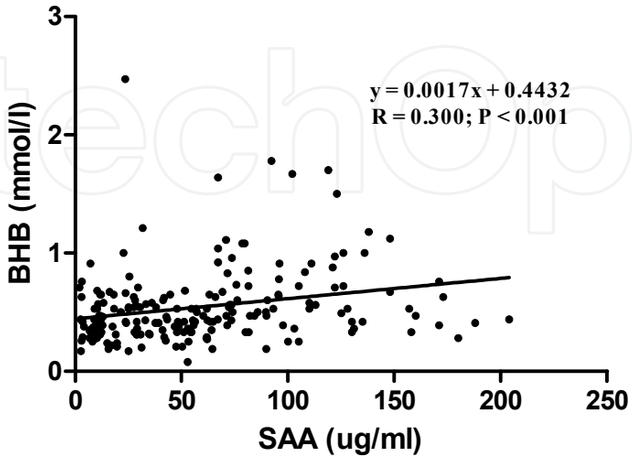


Fig. 7. Correlation and regression analysis between SAA and BHB concentrations

	Hp	SAA	Glu	TCH	TL	TG	NEFA	BHB
Hp	-	0.647^{c}	-0.247^{c}	-0.181^{a}	-0.137	-0.069	0.716^{c}	0.291^{c}
SAA	0.647^{c}	-	-0.249^{c}	-0.214^{c}	-0.041	-0.024	0.710^{c}	0.300^{c}
Glu	-0.247^{c}	-0.249^{c}	-	0.179^{a}	0.043	0.195^{b}	-0.27^{c}	-0.175^{a}
TCH	-0.181^{a}	-0.214^{b}	0.179^{a}	-	0.663^{c}	0.197^{b}	-0.125	-0.331^{c}
TL	-0.137	-0.041	0.043	0.663^{c}	-	0.205^{b}	-0.049	-0.196^{b}
TG	-0.069	-0.024	0.195^{b}	0.197^{b}	0.205^{b}	-	-0.093	-0.100
NEFA	0.716^{c}	0.710^{c}	-0.277^{c}	-0.125	-0.049	-0.093	-	0.320^{c}
BHB	0.291^{c}	0.300^{c}	-0.175^{a}	-0.331^{c}	-0.196^{b}	-0.100	0.320^{c}	-

a, b, c indexes show statistical significance of correlations: a – $P < 0.05$; b – $P < 0.01$; c – $P < 0.001$

Table 3. The correlations between selected acute phase proteins and variables of energetic metabolism

6.2 The concentrations of selected acute phase proteins during the reproduction cycle of sows

The results of the determination of selected acute phase proteins during the reproduction cycle of sows, characterized by average values (x), standard deviations (SD), and the statistical evaluation of the obtained results (P) are summarised in Tables 4 and 5.

In the Group I, by the evaluation of the serum concentrations of Hp we recorded in sows 2 weeks *ante partum* (2nd sample collection) markedly higher mean value compared with the 1st sampling (Table 4), However, the values differed not significantly. By other sample collections (*post partum*), there was a continuous decrease in its concentrations. In CRP concentrations, we found in sows by the 3rd and 4th sample collections nonsignificantly higher values compared with the 1st and 2nd samplings (Table 5). The highest average concentration of CRP was recorded in sows after farrowing (3rd sampling). The changes in average concentrations of Hp and CRP during the monitored period in this group of sows were not significant. All animals from this group were clinically healthy throughout the whole monitored period.

Groups of sows	Sample collection				ANOVA P
	1st	2nd	3rd	4th	
I	1.27 ± 0.45	2.30 ± 1.83	1.63 ± 0.40	1.57 ± 0.44	n. s.
II	1.76 ± 0.21^{a}	1.79 ± 0.44	1.63 ± 0.45	1.16 ± 0.16^{a}	n. s
III	2.96 ± 1.06^{a,b,B}	1.91 ± 0.65^{a,A}	1.27 ± 0.40^{b}	1.20 ± 0.59^{A,B}	< 0.01
IV	2.10 ± 0.68^{a,b}	1.44 ± 0.94	1.00 ± 0.71^{b}	0.99 ± 0.86^{a}	n. s.

The same indexes in lines mean statistical significance of differences in measured values between the groups of sows: a, A – $P < 0.05$; b, B – $P < 0.01$

P – significance of the differences in the obtained results, n. s. – non significant

Table 4. The changes in the concentrations of Hp (mg/ml) in blood serum of sows during different stages of reproduction cycle (x ± SD)

In the Group II, the analyses of the serum Hp concentrations showed no significant changes in its values from the period of 1 week before farrowing until 3 weeks after farrowing.

Significantly lower mean Hp concentrations compared with the 1st sampling was found 5 weeks after farrowing (4th sampling, $P < 0.05$). In the concentrations of CRP we found a nonsignificant increase of values by the 2nd and 3rd sample collection with consecutive more marked, but statistically not significant decrease of its average concentration bellow the level of initial values by the 4th sampling. The changes in the obtained results of Hp and CRP concentrations in this group of sows throughout the whole monitored period were not significant. All animals from this group were clinically healthy during the monitored period, and didn't exhibit changes in reproductive system after farrowing.

In the Group III, we recorded a trend to decrease Hp concentrations from the 1st (1 week *p.p.*) till the 4th sample collection (7 weeks *p.p.*). The mean value of Hp by the 1st sampling was significantly higher compared with its average concentrations recorded by the 3rd ($P < 0.05$) and 4th samplings ($P < 0.01$). The average Hp concentration in sows 3 weeks after farrowing (2nd sampling) was also significantly higher compared with the mean value obtained in animals by the 4th sampling ($P < 0.05$). Similarly, decreasing trend of values was found also in the concentrations of CRP. The average concentration of CRP in sows by the 1st sample collection was significantly higher compared with the mean value found by the 3rd sampling ($P < 0.05$). The changes in the concentrations of Hp and CRP in this group of sows during the monitored period were significant ($P < 0.01$ and $P < 0.05$). Almost in all of the animals from this group, clinical signs of mastitis-metritis-agalactia syndrome (MMA) were found by the 1st collection of specimens (1 week *p.p.*), characterized by a decreased food intake, discharge from vagina, erythema, and firmness of mammary gland. By the 2nd, 3rd and 4th sample collections, we did not record in these animals clinically evident changes in the reproductive system.

Group of the sows	Sample collection				ANOVA P
	1st	2nd	3rd	4th	
I.	16.27 ± 9.38	15.97 ± 12.35	27.19 ± 21.96	20.85 ± 10.16	n. s.
II.	23.97 ± 11.84	31.92 ± 37.20	49.98 ± 39.04	9.83 ± 7.36	n. s.
III.	64.92 ± 60.10^{a}	14.47 ± 14.82	7.78 ± 8.76^{a}	4.10 ± 3.39	< 0.05
IV.	23.59 ± 17.67^{a}	52.44 ± 48.27^{A}	8.25 ± 7.68^{a}	6.93 ± 12.91^{A}	< 0.05

The same indexes in lines mean statistical significance of differences in measured values between the groups of sows: a, A – $P < 0.05$

P – significance of the differences in the obtained results, n. s. – non significant

Table 5. The changes in the concentrations of CRP (ng/ml) in blood serum of sows during different stages of reproduction cycle (x ± SD)

In the Group IV, different changes in the concentrations of evaluated acute phase proteins were found. The analyses of serum Hp concentrations showed a trend of decreasing values. The concentrations of Hp by the 1st sample collection (1 week *post* weaning) were significantly higher compared with the values obtained by the 3rd and 4th samplings (5 and 7 weeks *post* weaning, $P < 0.05$). In the concentrations of C-reactive protein, after a non-significant increase of average value by the 2nd sampling, we recorded repeated decrease of

its values by the 3rd and 4th samplings. While the changes in the concentrations of Hp in this group of sows during the whole monitored period were not significant, the values of CRP showed significant changes throughout the monitored period ($P < 0.05$). By the 1st sample collection, we found in one animal from this group inflammatory changes on the carpal joint, the others were clinically healthy. The clinical examination of the evaluated animals by next samplings did not reveal any disorders of general health state.

Variable	Sample collections				ANOVA P
	4 weeks *a.p.*	**1 week** *a.p.*	**1 week** *p.p.*	**1 week** *p.***wean.**	
Hp	1.27 ± 0.45^{b}	2.09 ± 1.40	$2.17 \pm 0.93^{a,b}$	1.55 ± 0.64^{a}	n.s.
CRP	16.27 ± 9.38^{a}	19.17 ± 12.19	$42.52 \pm 44.34^{a,A}$	14.22 ± 14.05^{A}	< 0.05

The same indexes in lines mean statistical significance of differences in measured values between the groups of sows: a, A – $P < 0.05$; b – $P < 0.01$

P – significance of the differences in the obtained results, n. s. – non significant; a.p. – ante partum; p.p. – post partum;, p. wean. – post weaning

Table 6. The average concentrations of Hp and CRP in blood serum of sows in selected periods of reproduction cycle ($x \pm SD$)

A more detailed analysis of the individual concentrations of measured acute phase proteins from the evaluated groups of sows according to selected stages of reproduction cycle is summarised in Table 6. The highest average concentration of Hp (2.17 mg/ml) we found in sows 1 week after the farrowing. This value was significantly higher compared with average concentrations recorded in sows 4 weeks before parturition and 1 week after the weaning ($P < 0.01$ and $P < 0.05$, respectively). By the evaluation of the concentrations of CRP we found a similar trend of significantly increasing values with the highest mean value in sows 1 week *post partum*. While the differences in the concentrations of haptoglobin between the sows in different stages of reproduction cycle were not significant, in the values of C-reactive protein we found significant differences ($P < 0.05$).

7. Discussion

7.1 Relationships between acute phase proteins and altered energetic metabolism in dairy cows after calving

The immune system is significantly affected during pregnancy. There are significant interactions between the immune system and cells and tissues of the reproductive system that are critical for the maintenance of pregnancy, but are responsible for immune suppression that is associated with increased risk of diseases (Kehrli et al., 1990; Lippolis, 2008). Parturition with following metabolic challenges constitutes a potentially stressful event for the dairy cow. One of the ways how an animal can manifest its stress state is by activating its acute phase response, mainly by an increased production of acute phase proteins by the liver. According to Alsemgeest et al. (1993), the physiological processes taking place around the time of parturition are mainly responsible for higher concentrations of acute phase proteins in blood serum. Regassa & Noakes (1999) and Rottmann (2006) reported that higher values of acute phase proteins could be related to the tissue damage

occuring due to the increased myometrial activity during expulsion of the calf, involution of the uterus, as well as degeneration and regeneration of the endometrium. Young et al. (1995) found that higher concentrations of these proteins, determined in the last phase of pregnancy and after calving may be connected with the changing hormone profile (the influence of estrogens and progesterone). According to Alsemgeest et al. (1996), increased acute phase protein concentrations in cattle may be due to the increased concentrations of cortisol as part of the response to stress.

However, even if this response conserved it exhibit varations from one animal to another, some of them respond markedly, other have moderate or minor responses. Therefore, the differences between two groups of evaluated dairy cows, observed in our study in the concentrations of both measured acute phase proteins, may be due to numerous differences in the inflammatory responses to various external or internal stimuli. Pyörälä (2000) reported also that the production of acute phase proteins vary not only among different animal species, but also within them. Higher values of standard deviations obtained in both groups of cows reflect the different reactivity of acute phase proteins. The wider range of individual values of Hp, as well as SAA, suggests also the differences in the variability of animals reacting to both injury and impaired homeostasis.

Moreover, homeostais of all the energy substrates and the whole metabolism is altered during the time around parturition. Hardardottir et al. (1994) reported also that the acute phase response initiated by processes occuring around parturition is associated with numerous changes in lipid and glucose metabolism, such as decreased cholesterol, accelerated lipolysis, and increased NEFA concentrations in plasma. Investigations in human medicine showed that altered lipid metabolism, increased concentrations of non-esterified fatty acids in blood serum, and oxidative stress may markedly influence the systemic inflammatory response, and the development of inflammatory-based diseases (Sordillo et al., 2009). Our study showed highly positive correlation between the concentrations of Hp and SAA, as well as between both measured acute phase proteins and the concentrations of NEFA in dairy cows after calving. Kushibiki et al. (2002) stated that administration of tumor necrosis factor α to dairy cattle, promotes the production of acute phase proteins and is associated with decreased appetite and cachexia, and increased release of NEFA from adipose tissue into the plasma. Therefore, higher concentrations of non-esterified fatty acids in serum could be related to the activation of the immune system. Ametaj (2005) and Ametaj et al. (2005) reported that higher concentrations of haptoglobin and serum amyloid A after parturition correlate positively with total lipids in the liver, and proposed that fatty liver found in cows could be a response to non-specific inflammation associated to parturition.

The periparturient period is characterized by a sudden increase in energy requirements imposed by the onset of lactation and by a decrease in voluntary dry matter intake which results in negative energy balance (Leroy et al., 2008). A significant adaptation to the negative energy balance during the transition period is the mobilization of fat from body stores and the release of non-esterified fatty acids into the blood stream, which constitute important sources of energy in this period. Animals may react to these disturbances in their homeostasis and changes in metabolism with a set of physiological changes, including changes in the concentration of some plasma proteins, especially acute phase proteins. However, according to Bernabucci et al. (2005) and Sordillo et al. (2009), increased circulating NEFA concentrations are directly associated with increased systemic inflammatory conditions, and large amounts of adipose stores during time of energy

deficiency are linked with adverse health effects on the transition cow. Other authors demonstrated also a clear relationship among nutrition, inflammation and disease susceptibility, and that elevated NEFA concentrations are positive risk factors for many inflammatory periparturient diseases in dairy cows (Goff, 2006; Calder, 2008; Wood et al., 2009).

Highly significant positive correlation was found also between Hp, SAA and β-hydroxybutyrate, as well as between NEFA and BHB. These relationships may be explained by metabolic changes after parturition, since fat-derived substances are important sources of energy, because the majority of available glucose is redirected to the mammary gland for lactose synthesis (Herdt, 2000). However, further studies are needed to explain the aforementioned relationships with the immune response, characterized by changes in the concentrations of acute phase proteins in dairy cows after calving, and with the altered energetic metabolism.

Our study showed also a network of energetic metabolism factors, reflecting mutiple overlapping metabolic reactions, and physiological adaptations of the cow in the period after calving. Seifi et al. (2007) reported that after calving there is a positive correlation between NEFA and TG, as well as between NEFA and BHB. While between glucose and the other energetic profile factors no correlation was established.

7.2 The concentrations of selected acute phase proteins during the reproduction cycle of sows

Reproductive state and gravidity are important factors influencing most of the biochemical parameters of sows, including acute phase proteins (Lampreave et al., 1994; Verheyen et al., 2007). At present, physiological reference values for haptoglobin and C-reactive protein in pigs are not definitely established. However, it appeared that the time of sampling (before or after farrowing) has an important influence on most of the acute phase proteins.

Many researchers reported that concentrations of acute phase proteins undergo significant changes associated to parturition (Alsemgeest et al., 1993; Ametaj, 2005). In horses and cows the highest concentrations of major acute phase proteins were observed at day 1 *post partum* (Gymnich et al., 2003). Data from sows during parturition are lacking. Our results suggest that in sows there are also important changes in the concentrations of acute phase proteins associated to the reproduction cycle. In sows, at the week 1 after farrowing, significantly higher average concentrations of Hp, as well as CRP were found, as compared with samples analyzed before and later after parturition. Kostro et al. (2003) reported similar findings. According to Verheyen et al. (2007), serum Hp concentrations showed a significant increase one week after farrowing over 2.09 g/l. On the other hand, the aforementioned authors reported that, similarly to our results, the concentrations of Hp on the 94th and 108th day of gestation are roughly uniform (1.36 and 1.54 g/l). The increased Hp concentration *post partum* could be explained by physiological events during the *puerperium*. Moreover, higher values of Hp and CRP, recorded after parturition, may be consequences of increased cortisol production in adrenal cortex, as part of the response of the organism to stress (Uchida et al., 1993; Burger et al., 1998). According to Busch et al. (2003), Hp concentrations in young sows increase 2–8 weeks before farrowing, and the elevations are higher than in older sows. Verheyen et al. (2007) reported also that parity one sows showed higher Hp concentrations. This finding is in contrast whit the results presented by Petersen *et al*. (2002), who reported an increase in concentrations of acute phase proteins with age.

The reproductive tract of sows is susceptible to infection after farrowing because of the periparturient increase in the number of both nonpathogenic microflora and facultative pathogens in the caudal vagina and urinary bladder (Bilkei et al., 1994). Elevated concentrations of Hp and CRP in sows may reflect the inflammation in the reproductive tract and mammary gland. Mirko & Bilkei (2004) evaluated sows without postparturient complications of normal process of *puerperium* and sows suffering from MMA syndrome after parturition. In both groups they recorded an increase of the concentrations of Hp and α_1-acid glycoprotein in postparturient period. The concentrations of the aforementioned acute phase proteins on the 1st and 5th day after parturition were higher in sows suffering from MMA syndrome compared with sows without clinical signs of reproductive disorders. Friendship & Bilkei (2005) stated that in sows with MMA syndrome and other urogenital diseases the Hp concentrations were higher on the 1st and 5th day of lactation. Therefore, monitoring the concentrations of these indicators during the first days after parturition may be used to diagnose early stages of the MMA syndrome and to start suitable therapy (Gymnich et al., 2003).

In general, the acute phase response is considered to be useful tool in prevention of microbial growth, and may help in recovery of the organism. In addition, an active cell immune response in sow, indirectly negatively influence growth rate in preweaning piglets, probably due to decreased milk production (Bilkei, 1995; Segales et al., 2004).

8. Conclusion

Our present results indicate strong relationships between acute phase proteins and some variables of energetic metabolism in cows shortly after parturition. In this critical period, we recorded significant correlations between evaluated acute phase proteins and non-esterified fatty acids, as well as β-hydroxybutyrate. Understanding how all these factors interact with the immune system will help in developing disease control and management strategies that will aid in maintaining good health in dairy cattle, resulting in greater production.

The aforementioned results suggest that acute phase proteins, haptoglobin and serum amyloid A, may be potential candidates for monitoring the around parturition time. However, future possibilities for acute phase reactants depend on basic new molecular mechanims involving known proteins, as well as new discoveries such as organ-specific components, and new technological possibilities for rapid immunological or chemical multi-analyses.

The aforementioned results suggest that the reproductive state influences the production of acute phase proteins, and indicates that around parturition in sows there are important changes in the concentrations of diagnostically useful acute phase proteins. In the monitored period we recorded significant changes in the values of haptoglobin and C-reactive protein with their highest concentrations shortly after parturition. However, the interpretation of these metabolites should always be performed together with a thorough anamnesis and clinical evaluation of individual animals.

The advantages and uses of acute phase protein assays are well supported in the human medicine. Unfortunately, because of the practical limitations of current technology, clinical application of acute phase protein analyses in veterinary medicine is not widespread. Continuing challenges include the need for automated assays and standardization of tests across laboratories. However, many potential uses are possible for acute phase protein measurements to assess the health state, poor hygiene and welfare in pig production processes. In addition, acute phase proteins seem to be a promising marker of health status by reflecting a

broad spectrum of ongoing clinically declared, as well as asymptomatic diseases. Exceptionally sensitive, but non-specific markers of diverse inflammatory etiologies, acute phase proteins are excellent candidates to monitor both animal health, and animal wellbeing.

9. Acknowledgment

This work was supported by VEGA Scientific Grant No 1/0614/09 from the Ministry of Education, and by Slovak Research and Development Agency under contract No. APVV-0475-10.

10. References

Alsemgeest, S.P.M., Taverne, M.A.M., Boosman, R., van der Weyden, B. & Gruys, E. (1993). Peripartum acute-phase protein serum amyloid-A concentration in plasma of cows and fetuses, *American Journal of Veterinary Research*, Vol.54, pp. 164-167

Alsemgeest, S.P.M., vant Clooster, G.A.E., van Miert, A.S.J.P.A.M., Huslkamp-Koch, C.K. & Gruys, E. (1996). Primary bovine hepatocytes in the study of cytokine induced acute-phase protein secretion *in vitro*, *Veterinary Immunology and Immunopathology,* Vol.53, pp. 179-184

Ametaj, B. (2005). A new understanding of the causes of fatty liver in dairy cows, *Advances in Dairy Technology*, Vol.17, pp. 97-112

Ametaj, B.N., Bradford, B.J., Bobe, G., Nafikov, R.A., Lu, Y., Young, J.W. & Beitz, D.C. (2005). Strong relationships between mediators of the acute phase response and fatty liver in dairy cows, *Canadian Journal of Animal Sciences*, Vol.85, pp. 165-175

Baumann, H. & Gauldie, J. (1994). The acute phase response, *Immunology Today*, Vol.15, pp. 74-80

Bellomo, R. (1992). The cytokine network in the critically ill, *Anaesthesia and Intensive Care*, Vol.20, pp. 288-302

Berkova, N., Lemay, A., Dresser, D.W., Fontaine, J.Y., Kerizit, J. & Goupil, S. (2001). Haptoglobin is present in human endometrium and shows elevated levels in the decidua during pregnancy, *Molecular Human Reproduction*, Vol.7, pp. 747-754

Bernabucci, U., Ronchi, B., Lacetera, N. & Nardone, A. (2005). Influence of body condition score on relationships between metabolic status and oxidative stress in periparturient dairy cows, *Journal of Dairy Science*, Vol.88, pp. 2017-2026

Bilkei, G. (1995). Herd health strategy for improving the reproductive performance of pigs, *Proceedings of the 8th „In-between" Symposium of the International Society for Animal Hygiene, Hungarian Veterinary Journal*, Vol.10, pp. 766-768

Bilkei, G., Bölcskei, A. & Goos, T. (1994). Bericht über den peripartalen Krankheitskomplex der Muttersau in der industriellen Schweinezucht. 1ste Mitteilung: Peripartaler Verlauf der Bakteriurie der Sauen mit vaginal-vulvalem Ausfluss in einem modernen Schweinezuchtbetrieb, *Berliner und Münchener Tierärztliche Wochenschrift,* Vol.107, pp. 327-330

Burger, W., Ewald, C. & Fennert, E.M. (1998). Increase in C-reactive protein in the serum of piglets (pCRP) following ACTH or corticosteroid admimistration, *Journal of Veterinary Medicine Series B*, Vol.45, pp. 1-6

Busch, M.E., Baekbo, P. & Wachmann, H. (2003). Haptoglobin levels in sows and associations with clinical signs of disease around farrowing, *Proceedings of the Fourth European Colloquium on Acute Phase Proteins,* p. 33, Segovia, Spain

Cai, T.Q., Weston, P.G., Lund, L.A., Brodie, B., McKenna, D.J. & Wagner, W.C. (1994). Association between neutrophil functions and periparturient disorders in cows, *American Journal of Veterinary Research*, Vol.55, pp. 934-943

Calder, P.C. (2008). The relationship between the fatty acid composition of immune cells and their function, *Prostaglandins Leukotrienes and Essential Fatty Acids*, Vol.79, pp. 101-108

Cray, C., Zaias, J. & Altman, N.H. (2009). Acute phase response in animals : a review, *Comparative Medicine*, Vol.59, No.6, pp. 517-526

Du Clos, T.W. (2004). C-reactive protein. An activator of innate imunity and a modulator of adaptive imunity, *Immunolological Research*, Vol.30, pp. 261-277

Eckersall, P.D. (2000). Recent advances and future prospects for the use of acute phase proteins as markers of disease in animals, *Revue de Médicine Véterinarie*, Vol.151, No.7, pp. 577-584

Eckersall, P.D. & Bell, R. (2010). Acute phase proteins : Biomarkers of infection and inflammation in veterinary medicine, *The Veterinary Journal*, Vol.185, pp. 23-27

Friendship, P.Z.E. & Bilkei, G. (2005). Acute phase proteins and serum cortisol levels in sows affected with mastitis, metritis, agalactia (MMA) and swine urogenital disease (SUGD), *The Pig Journal*, Vol.55, pp. 9-18

Gatzka, C., Bremerich, D., Kaufmann, M. & Ahr, A. (2002). Isolated decrease in haptoglobin during pregnancy: diagnosis by chance or pathological? *Zentralblatt für Gynakologie*, Vol.124, pp. 120-122

Glock, X.T.P. & Bilkei, G. (2005). The effect of postparturient urogenital diseases on the lifetime reproductive performance of sows, *Canadian Veterinary Journal*, Vol.46, pp. 1103-1107

Goff, J.P. (2006). Major advances in our understanding of nutritional influences on bovine health, *Journal of Dairy Science*, Vol.89, pp. 1292-1301

Gruys, E., Touissant, M.J.M., Landman, W.J.M., Tivapasi, M., Chamanza, R. & van Veen, L. (1999). Infection, inflammation and stress inhibit growth. Mechanism and non-specific assessment of the processes by acute phase proteins, In: *Production diseases in farm animals*, T. Wensing (Ed.), 72-87, Wageningen Press, The Netherlands

Gruys, E., Toussaint, M.J.M., Niewold, T.A. & Koopmans, S.J. (2005). Acute phase reaction and acute phase proteins, *Journal of Zhejiang University Science*, Vol.6B, No.11, pp. 1045-1056, ISSN 1009-3095

Gymnich, S., Hiss, S., Sauerwein, H. & Petersen, B. (2003). Haptoglobin in sows at parturition, *Proceedings of the Fourth European Colloquium on Acute Phase Proteins,* p. 136, Segovia, Spain

Hachanberg, S., Weinkauf, C., Hiss, S. & Sauerwein, H. (2007). Evaluation of classification modes potentially suitable to identify metabolic stress in healthy dairy cows during the peripartal period, *Journal of Animal Sciences*, Vol.85, pp. 1923-1932

Hardardottir, I., Grunfeld, C. & Feingold, K.R. (1994). Effects of endotoxin and cytokines on lipid metabolism, *Current Opinion in Lipidology*, Vol.5, pp. 207-215

Herdt, T.H. (2000). Ruminants adaptation to negative energy balance. Influences on the etiology of ketosis and fatty liver, *Veterinary Clinics of North America: Food Animal Practice,* Vol.16, pp. 215-230

Jackson, P.G.G. & Cockcroft, P.D. (2002). *Clinical examination of farm animals.* Blackwell Science Ltd., Blackwell Publishing Company, ISBN 0-632-05706-8, Oxford, United Kingdom

Jacobsen, S. (2003). The bovine acute phase response to endotoxin and Gram-negative bacteria, Ph.D. thesis, 162 pp., Samfundslitteratur Grafik, Frederiksberg, Denmark

Janeway, C.A., Travers, P., Walport, M. & Schlomschik, M.J. (2001). *Immunobiology,* 5th ed., Taylor & Francis, London, United Kingdom

Johnson, R.W. (1997). Inhibition of growth by pro-inflammatory cytokines; an integrated view, *Journal of Animal Science*, Vol.75, pp. 1244-1255

Kehrli, M.E.Jr., Goff, J.P., Harp, J.A., Thurston, J.R. & Norcross, N.L. (1990). Effects of preventing periparturient hypocalcemia in cows by parathyroid hormone administration on hematology, immunoglobulin, and shedding of *Staphylococcus aureus* in milk, *Journal of Dairy Science,* Vol.73, pp. 2103-2111

Koj, A. (1996). Initiation of acute phase response and synthesis of cytokines, *Biochemical and Biophysical Acta,* Vol.1317, pp. 84-94

Kostro, K., Wawron, W., Szczubial, M., Luft-Deptula, D. & Glinski, Z. (2003). C-reactive protein in monitoring and evaluation of effects of therapy of the MMA syndrome of sows, *Polish Journal of Veterinary Science*, Vol.6, pp. 235-238

Krakowski, L. & Zdzisińska, B. (2007). Selected cytokines and acute phase proteins in heifers during the ovarian cycle course and in different pregnancy periods, *Bulletin of the Veterinary Institue Pulawy*, Vol.51, pp. 31-36

Kushibiki, S., Hodate, K., Shingu, H., Hayashi, T., Touno, E., Shimoda, M. & Yokomizo, Y. (2002). Alterations in lipid metabolism induced by recombinant bovine tumor necrosis factor-alpha administration in dairy heifers, *Journal of Animal Sciences,* Vol.80, pp. 2151-2157

Lampreave, F., Gonzalez-Ramon, N., Martinez-Ayensa, S., Hernandez, M.-A., Lorenzo, H.-K., Garcia-Gil, A. & Pineiro, A. (1994). Characterisation of the acute phase serum protein response in pigs, *Electrophoresis*, Vol.15, pp. 672-676

Lauritzen, B., Lykkesfeldt, J., Skaanild, M.T., Angen, Ø., Nielsen, J.P. & Friis, C. (2003). Putative biomarkers for evaluating antibiotic treatment of *Actinobacillus pleuropneumoniae* infection in pigs, *Research in Veterinary Science*, Vol.74, pp. 271-277

Leroy, J.I., Vanholder, T., Van Knegsel, A.T., Garcia-Ispierto, I. & Bols, P.E. (2008). Nutrient prioritization in dairy cows early postpartum: mismatch between metabolism and fertility. *Reproduction in Domestic Animals*, Vol.43, pp. 96-103

Lippolis, J.D. (2008). Immunological signaling networks: integrating the body's immune response, *Journal of Animal Sciences*, Vol.86, pp. E53-E63

Marnell, L., Mold, C. & Du Clos, T.W. (2005). C-reactive protein: Ligands, receptors and role in inflammation, *Clinical Immunology*, Vol.117, pp. 104-111

Mirko, C.P. & Bilkei, G. (2004). Acute phase proteins, serum cortisol and preweaning litter performance in sows suffering from periparturient disease, *Acta Veterinaria Beograd*, Vol.54, pp. 153-161

Moberg, G.P. (2000). Biological response to stress: Implications for animal welfare, In: *The Biology of Animal Sress*, G.P. Moberg & J.A. Mench (Eds.), 1-21, CABI Publishing, New York, USA

Murata, H., Shimada, N. & Yoshioka, M. (2004). Current research on acute phase proteins in veterinary diagnosis : an overview, *The Veterinary Journal*, Vol.168, pp. 28-40

Petersen, H.H., Ersbøll, A.K., Jensen, C.S. & Nielsen, J.P. (2002). Serum haptoglobin concentration in Danish slaughter pigs in different health status, *Preventive Veterinary Medicine,* Vol.54, pp. 325-335

Petersen, H.H., Nielsen, J.P. & Heegaard, P.M.H. (2004). Application of acute phase protein measurements in veterinary clinical chemistry, *Veterinary Research*, Vol.35, pp. 136-187

Pyörälä, S. (2000). *Hirvonen's thesis on acute phase response in dairy cattle*, University of Helsinki, ISBN 951-45-9104-6, Helsinki, Finnland

Reese, D.E., Peo, E.R., Lewis, A.J. & Hogg, A. (1984). Serum chemical values of gestating and lactating swine: reference values, *American Journal of Veterinary Research*, Vol.45, pp. 978-980

Regassa, F. & Noakes, D.E. (1999). Acute phase protein response of ewes and the release of PGFM in relation to uterine involution and the presence of intrauterine bacteria.,*Veterinary Record*, Vol.144, pp. 502-506

Rottmann, S. (2006). *Einfluss von nichtsteroidalen Antiphlogistika (NSAID) auf hämatologische und klinisch-chemische Parameter bei Rindern mit Dystokie,* Inaugural-Dissertation, Veterinärmedizinische Fakultät der Universität Leipzig, Leipzig, Germany

Segales, J., Pineiro, C., Lampreave, F., Nofrarias, M., Mateu, E., Calsamiglia, M., Andres, J., Morales, M., Pineiro, M. & Domingo, M. (2004). Haptoglobin and pig-major acute protein are increased in pigs with postweaning multisystemic wasting syndrome (PMWS), *Veterinary Research*, Vol.35, pp. 275-282

Seifi, H.A., Gorji-Dooz, M., Mohri, M., Dalir-Naghaden, B. & Farzaneh, N. (2007). Variations of energy-related biochemical metabolites during transition period in dairy cows, *Comparative Clinical Pathology*, Vol.16, pp. 253-258

Skinner, J.G., Brown, R.A.L. & Roberts, L. (1991). Bovine haptoglobin response in clinically defined field conditions, *Veterinary Record*, Vol.128, pp. 147–149

Sordillo, L.M., Contreras, G.A. & Aitken, S.L. (2009). Metabolic factors affecting the inflammatory response of periparturient dairy cows, *Animal Health Research Revue,* Vol.10, pp. 53-63.

Thornton, E.J., Wilson, R.J. & Connaughton, I. (1998). Effect of subclinical urogenital infection on reproductive performance in the sow, *Proceedings of the 15th International Pig Veterinary Society Congress,* p.236, Birmingham, England

Toussaint, M.J.M., Eckersall, P.D., Alava, M., Madec, F., Meleon, R.H. & Gruys, E. (2000). Acute phase protein assays as tool in assessment of health in pigs, *Revue de Medicine Veterine*, Vol.151, pp. 780

Uchida, E., Katoh, N. & Takahashi, K. (1993). Appearance of haptoglobin in serum from cows at parturition, *Journal of Veterinary Medical Science*, Vol.55, pp. 893-894

Yaqoob, P. & Calder, P.C. (2007). Fatty acids and immune functions: new insights into mechanisms, *British Journal of Nutrition*, Vol.98, pp. S41-S45

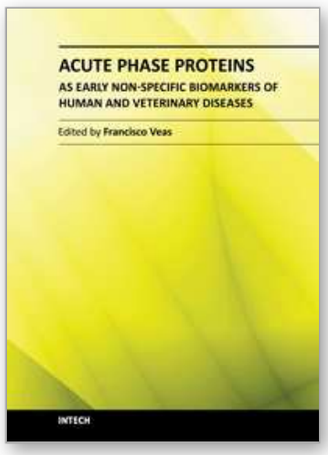
Young, C.R., Eckersall, P.D., Saini, P.K. & Stanker, L. (1995). Validation of immunoassays for bovine haptoglobin, *Veterinary Immunology and Immunopathology*, Vol.49, pp. 1-13

Verheyen, A.J.M., Maes, D.G.D., Mateusen, B., Deprez, P., Janssens, G.P.J., de Lange, L. & Counotte, G. (2007). Serum biochemical reference values for gestating and lactating sows, *The Veterinary Journal*, Vol.174, pp. 92-98

Waller, C.M., Bilkei, G. & Cameron, R.D.A. (2002). Effect of periparturient disease and/or reproductive failure accompained by excessive vulval discharge and weaning to mating interval on sow reproductive performance, *Australian Veterinary Journal,* Vol.80, pp. 545-549

Whicher, J.T. & Westacott, C.I. (1992). The acute phase response, In: *Biochemistry of inflammation,* J.T. Whicher & S.W. Evans, (Eds.), 243-271, Kluwer Academic, London, United Kingdom

Wood, I.G., Scott, H.A., Garg, M.I. & Gibson, P.G. (2009). Innate immune mechanisms linking non-esterified fatty acids and respiratory disease, *Progress in Lipid Research,* Vol.48, pp. 27-43



Acute Phase Proteins as Early Non-Specific Biomarkers of Human and Veterinary Diseases

Edited by Prof. Francisco Veas

ISBN 978-953-307-873-1
Hard cover, 408 pages
Publisher InTech
Published online 10, October, 2011
Published in print edition October, 2011

The two volumes of Acute Phase Proteins book consist of chapters that give a large panel of fundamental and applied knowledge on one of the major elements of the inflammatory process during the acute phase response, i.e., the acute phase proteins expression and functions that regulate homeostasis. We have organized this book in two volumes - the first volume, mainly containing chapters on structure, biology and functions of APP, the second volume discussing different uses of APP as diagnostic tools in human and veterinary medicine.

How to reference

In order to correctly reference this scholarly work, feel free to copy and paste the following:

Gabriel Kováč, Csilla Tóthová, Oskar Nagy and Herbert Seidel (2011). Acute Phase Proteins in Dairy Cows and Sows During the Periparturient Period, Acute Phase Proteins as Early Non-Specific Biomarkers of Human and Veterinary Diseases, Prof. Francisco Veas (Ed.), ISBN: 978-953-307-873-1, InTech, Available from: http://www.intechopen.com/books/acute-phase-proteins-as-early-non-specific-biomarkers-of-human-and-veterinary-diseases/acute-phase-proteins-in-dairy-cows-and-sows-during-the-periparturient-period

INTECH
open science | open minds

InTech Europe
University Campus STeP Ri
Slavka Krautzeka 83/A
51000 Rijeka, Croatia
Phone: +385 (51) 770 447
Fax: +385 (51) 686 166
www.intechopen.com

InTech China
Unit 405, Office Block, Hotel Equatorial Shanghai
No.65, Yan An Road (West), Shanghai, 200040, China
中国上海市延安西路65号上海国际贵都大饭店办公楼405单元
Phone: +86-21-62489820
Fax: +86-21-62489821

IntechOpen