Japanese Journal of Veterinary Research 73(2): 36–43, 2025

JJVR

SHORT COMMUNICATION Experimental Research

Comparison of serum haptoglobin and procalcitonin in calves with bovine respiratory disease

Tomoko Koshiishi[1)], Keiichi Hisaeda[2)], Masanobu Nasu[3)], Shusaku Shibutani[1,*)] and Hiroyuki Iwata[1,*)]

[1)] Laboratory of Veterinary Hygiene, The United Graduate School of Veterinary Science, Yamaguchi University, 753-8515, Yamaguchi, Japan
[2)] Department of Veterinary Medicine, Okayama University of Science, 794-8555, Ehime, Japan
[3)] Higashiuwa Agricultural Cooperative Association, 797-1211, Ehime, Japan

Received for publication, September 30, 2024; accepted, April 22, 2025

Abstract

Bovine respiratory disease (BRD) significantly impacts the beef and dairy industries. The acute phase proteins procalcitonin (PCT) and haptoglobin (Hp) have been proposed as useful biomarkers for BRD. Here, we examined the time course of these two biomarkers in BRD-affected calves and their relationship to prognosis. Hp and PCT were elevated on the 1st day of examination (day 1). The PCT value on day 1 showed a positive correlation with the BRD score on day 7. Therefore, serum PCT concentration on day 1 may be used to predict whether symptoms are present on day 7. This study provides useful insights into the use of PCT and Hp in the diagnosis of BRD, particularly the use of PCT to determine prognosis.

Key Words: Fbovine respiratory disease, haptoglobin, procalcitonin

Bovine respiratory disease (BRD) is a disease caused by the combined effects of infection with pathogens, such as viruses and bacteria, and environmental stress. BRD is a major cause of mortality in cattle and has a significant impact on the beef and dairy industries[23,31)]. Therefore, the development and validation of methods for BRD diagnosis and prognosis is important. Given the complexity of the pathogenesis of BRD, it is important to appropriately use biomarkers with different reactivity to more accurately assess the pathogenesis. One potential biomarker is procalcitonin (PCT). PCT is a specific biomarker for bacterial infection that is elevated by stimulation with interleukin-1β (IL-1β), tumor necrosis factor-α (TNFα), and lipopolysaccharide (LPS)[14,16,25)]. In cattle, serum PCT has been reported to be a useful biomarker as it is elevated in cases of sepsis[2)], septicemic colibacillosis[11)], systemic inflammatory response syndrome (SIRS)[7)], mastitis[22)], and

* Corresponding author:
Shusaku Shibutani
Laboratory of Veterinary Hygiene, The United Graduate School of Veterinary Science, Yamaguchi University, 753-8515, Yamaguchi, Japan
Tel and Fax: +81-83-933-5900
E-mail: shushibu@yamaguchi-u.ac.jp
Hiroyuki Iwata
Laboratory of Veterinary Hygiene, The United Graduate School of Veterinary Science, Yamaguchi University, 753-8515, Yamaguchi, Japan
Tel and Fax: +81-83-933-5899
E-mail: hiwata@yamaguchi-u.ac.jp
doi: 10.57494/jjvr.73.2_36

BRD[10]. We previously demonstrated that the presence or absence of serum PCT was associated with BRD-related symptoms persistence in calves, suggesting that PCT may be a useful biomarker for BRD prognosis[15], suggesting that measuring serum PCT levels may be a useful method to assess bacterial infection in BRD. In addition, haptoglobin (Hp) is known to be a major acute phase protein in cattle and is elevated in response to trauma, non-infectious inflammation, viral infection, and bacterial infection[19,24]. It is also considered useful in the diagnosis of BRD[10,20,30]. Since secondary bacterial infection may contribute to the progression of the disease even when the primary cause of BRD is a viral infection[13], Hp and PCT may show different responses and time courses in BRD. However, there are no reports examining the relationship between clinical symptoms and PCT or Hp in BRD calves. In this study, we investigated the characteristics of Hp and PCT as biomarkers in calves affected by BRD by comparing the kinetics of their serum concentrations, correlation with prognosis, and association with clinical symptoms.

The study population consisted of 22 calves aged 157–399 d that were raised at three farms in Ehime Prefecture, Japan. The study period spanned from December 2013 to February 2016, during which time the calves were found by their owners to exhibit abnormalities and were subsequently diagnosed with BRD by 0 to 1 day later. Twenty-two BRD-affected calves comprising 13 Japanese black calves and 9 Japanese black/Holstein hybrid (F1) calves were examined. The control group comprises five healthy F1 calves (105–127 day old) raised at one of the aforementioned farms. For the BRD group, physical examination, auscultation, and BRD scores were measured on day 1 for diagnosis. The BRD score was defined based on the presence of eye discharge (scored as 0 or 2), nasal discharge (0 or 4), ear drop or head tilt (0 or 5), cough (0 or 2), respiration quality (normal/rapid or difficult breathing) (0 or 2), and rectal temperature (0 or 2; ≥39.2°C), considering California BRD Scoring System[3]. A BRD score of 5 or higher has been proposed as a value for BRD diagnosis[17]. On day 1, 18 of the 22 calves exhibited a BRD score of ≥5, and the other four calves had a BRD score of 4. The BRD scores were reassessed on days 2, 3, and 7. Treatment with antimicrobials was initiated and no other drugs such as anti-inflammatory agents were used. The number of treatment cycles was 4.2 ± 0.9 (2 to 9 times), and the outcome was a cure after treatment.

Blood samples were collected from the jugular vein of calves on days 1, 2, 3, and 7. Blood smears were prepared from heparin-treated whole blood samples, and leukocytes were classified and analyzed using an automated cell counter (KX-21NV; Sysmex, Kobe, Japan). Serum samples were prepared by centrifuging heparin-free whole blood at 2,500 × g for 20 min at 4°C. The serum samples were stored at –20°C until analysis. Serum Hp concentrations were measured using a bovine haptoglobin enzyme-linked immunosorbent assay (ELISA) test kit (Life Diagnostics, Inc., West Chester, PA, USA). Serum PCT concentrations were measured using the bovine Procalcitonin ELISA kit (Cusabio Biotech, Houston, TX, USA). The data obtained were subjected to statistical analysis using GraphPad Prism 7 version 7.0e (GraphPad Software, San Diego, CA, USA) or R version 4.2.1[28]. On day 1, specimens were collected from the right and left nasal cavities of 11 BRD-affected calves using sterile swabs, plated on 5% sheep blood agar plates (Nissui, Tokyo, Japan), and incubated aerobically at 37°C for 24 h. *Pasteurella multocida* and *Mannheimia haemolytica* were identified by microscopic observation after Gram staining and ID Test HN-20 Rapid (Nissui) according to the analytical profile of the kit; *Streptococcus* spp. were confirmed by microscopic observation after Gram staining and a negative catalase test. Antigen tests for infectious bovine rhinotracheitis virus (IBRV), bovine parainfluenza virus type 3 (PI-3), and bovine respiratory syncytial virus (BRSV) were obtained from the Nanyo Animal Health Center, Yawatahama Branch, Nanyo District Bureau, Ehime Prefecture.

Calves in the BRD group had a body temperature of 40.4 ± 0.2°C, heart rate of 114.8 ± 7.0 /min, respiratory rate of 65.3 ± 5.3 /min,

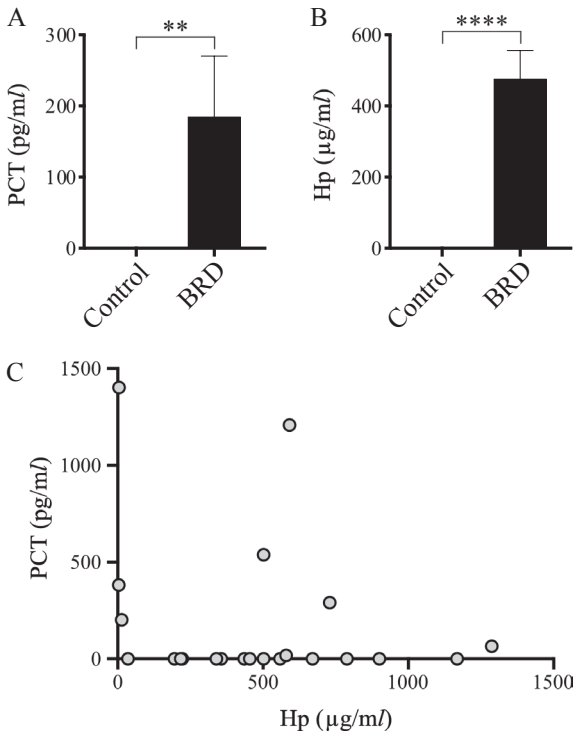

Fig. 1. Serum concentrations of procalcitonin (PCT) and haptoglobin (Hp) in healthy control calves and calves with bovine respiratory disease (BRD) on day 1 of examination.

(A) Serum PCT concentrations in control (n = 5) and BRD-affected calves (n = 22) on day 1 of examination. Serum concentrations are presented as mean ± SE. **: P <0.01 (Brunner–Munzel test).

(B) Serum Hp concentrations of control (n = 5) and BRD-affected calves (n = 22) on day 1 of examination. Serum concentrations are presented as mean ± SE. ****: P <0.0001 (Mann-Whitney U test).

(C) Plot of serum Hp versus serum PCT concentrations on day 1 of BRD-affected calves' examination (n = 22).

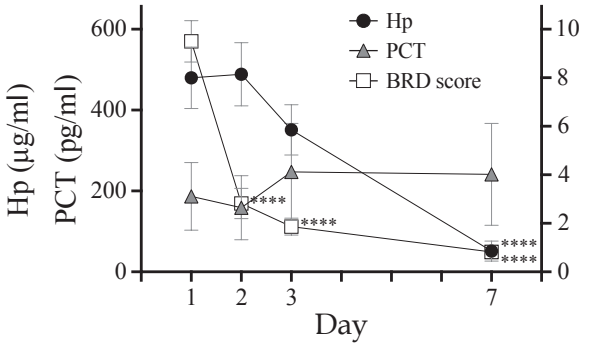

Fig. 2. Changes in serum procalcitonin (PCT), haptoglobin (Hp), and bovine respiratory disease (BRD) scores in calves with BRD.

Time course of PCT, Hp, and BRD score in 22 BRD-affected calves.

Hp **** (day 7): P < 0.0001 (Dunnett's test, compared to Hp concentration on day 1).

BRD score **** (days 2, 3, and 7): P < 0.0001 (Kruskal-Wallis test, compared to BRD score on day 1).

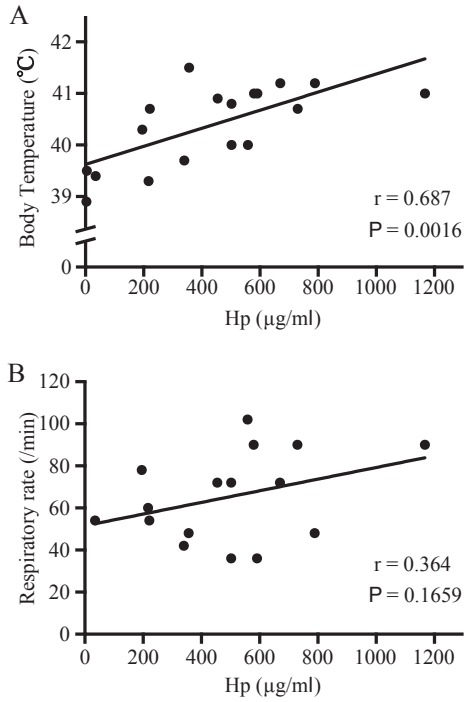

Fig. 3. Correlation between serum Hp concentration, body temperature, and respiratory rate on day 1.

(A) Plot of serum Hp concentration versus body temperature (rectal temperature) on day 1 (n = 18). (B) Plot of serum Hp concentration versus respiratory rate on day 1 (n = 16).

r: Pearson's product-moment correlation coefficient.

and BRD score of 9.5 ± 0.9 on day 1. Abdominal respiration was observed in 22.7% of the calves and oral respiration in 9.1%. Auscultation revealed abnormal respiratory sounds such as wheezing (31.8%), rhonchi (9.1%), fine crackles (9.1%), coarse crackles (4.5%), increased bronchial sounds (22.7%), and pleural friction rub (4.5%). The five healthy calves in the control group exhibited low serum Hp (2.7 ± 0.2 μg/ml) levels and serum PCT concentrations below the detection limit (PCT = 0 pg/ml). In contrast, on day 1, the serum PCT and Hp concentrations of the 22 calves in the BRD group (186.6 ± 83.5 pg/ml and 479.8 ± 75.7 μg/ml, respectively) were significantly higher than those in the control group (Fig. 1A and B). When serum PCT concentration was plotted against serum Hp concentration in individual cases (Fig. 1C), no significant correlation was

Table 1. Values of general physical examination, blood tests, bovine respiratory disease (BRD) scores and their comparison with procalcitonin (PCT) and haptoglobin (Hp) day 1 values in BRD affected calves.

Parameter	Reference value [8,12,27]	Value in BRD-affected calves (day 1 value except for BRD score)	vs. day 1 PCT		vs. day 1 Hp	
			Correlation coefficient	P value	Correlation coefficient	P value
Temperature (˚C)	38-39	40.4 ± 0.2	-0.11	0.663	0.732	0.000549
Respiration (min)	12-36	65.3 ± 5.3	0.0906	0.739	0.261	0.329
WBC (/μl)	4000-12000	9276.2 ± 520.2	-0.0097	0.967	-0.438	0.0471
Neu (/μl)	600-4000	1864.8 ± 284.6	0.227	0.31	-0.0734	0.745
Band (/μl)	0-120	117.9 ± 37.3	0.176	0.434	0.292	0.187
Lym (/μl)	2500-7500	7175.2 ± 344.2	-0.185	0.411	-0.601	0.00369
Mon (/μl)	25-840	212.2 ± 49.2	-0.0559	0.805	-0.114	0.613
AST (IU/L)	43-127	57.4 ± 3.1	0.452	0.0348	-0.255	0.252
Alb (g/dL)	3.03-3.55	2.9 ± 0.2	-0.435	0.0553	0.0634	0.791
Albumin/Globulin	0.84-0.94	0.9 ± 0.2	-0.273	0.243	-0.147	0.534
Day 1 BRD score		9.8 ± 0.9	-0.0618	0.785	0.22	0.325
Day 7 BRD score		0.8 ± 0.3	0.611	0.00255	0.218	0.33

WBC: white blood cells, Neu: neutrophils, Band: band neutrophils, Lym: lymphocytes, Mon: monocytes, AST: aspartate aminotransferase, Alb: albumin.
Data represent mean ± SE.
Spearman's rank correlation coefficient.

Table 2. Results of nasal swab bacterial culture and viral antigen tests in 11 bovine respiratory disease (BRD)-affected calves and day 1 serum procalcitonin (PCT), haptoglobin (Hp), and BRD scores.

Detected pathogen(s)	Number of calves	PCT (pg/ml)	Hp (μg/ml)	BRD score
Pasteurella multocida	3	118.7 ± 87.8	972.5 ± 164.9	7.0 ± 3.0
Pasteurella multocida and *Streptococcus* spp.	5	107.6 ± 107.6	603.2 ± 170.6	11.0 ± 1.4
Pasteurella multocida, Streptococcus spp., and BRSV	2	604.1 ± 604.1	523.0 ± 68.2	14.0 ± 1.0
Not detected	1	Below detection limit	558.8	13.0

BRSV: bovine respiratory syncytial virus.
Data represent mean ± SE.

observed between PCT and Hp (r = –0.100, P = 0.6593). The changes in serum PCT, Hp, and BRD scores during the survey period for BRD-affected calves are shown in Figure 2. Serum Hp in the BRD group decreased significantly on days 3 and 7 compared to day 1. On the other hand, serum PCT in the BRD group did not change significantly during the study period, and the BRD score in the BRD group decreased significantly on days 2, 3, and 7 compared to day 1. Although serum Hp concentration in the BRD group was positively correlated with body temperature (rectal temperature) on day 1 (r = 0.687, P = 0.0016) (Fig. 3A), there was no significant correlation between serum Hp concentration and respiratory rate (r = 0.364, P = 0.1659) (Fig. 3B). There was also no significant correlation between PCT and temperature or respiratory rate (r = –0.110, P = 0.6627; r = 0.091, P = 0.7387, respectively). Serum Hp on day 1 in the BRD group was negatively correlated with the white blood cell count and lymphocyte count on day 1 (r = -0.438, P = 0.0471, r = -0.601, P = 0.00369, respectively) (Table 1), and serum PCT on day 1 in the BRD group showed weak correlation with serum aspartate aminotransferase (AST) on day 1 (r = 0.452, P = 0.0348) (Table 1). Low serum albumin levels were found in BRD affected calves, although not correlated with Hp and PCT (Table 1). Other parameters were not significantly associated with Hp and PCT. Results of nasal swabs from 11 animals for causative pathogens and serum PCT, Hp, and BRD scores for each detected pathogens are shown in Table 2. Due to the small sample

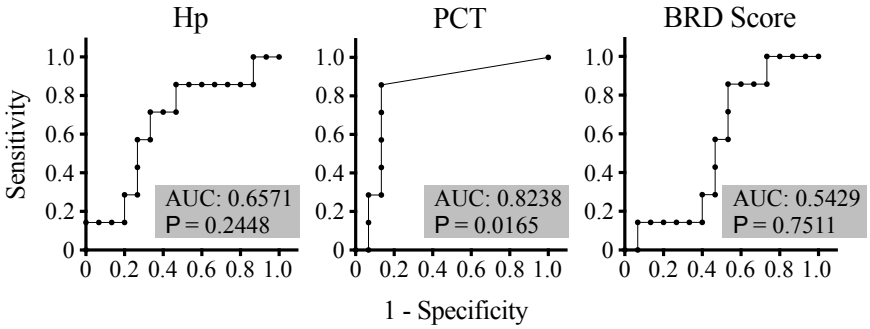

Fig. 4. Prediction of symptom presence/absence on day 7 using serum haptoglobin (Hp) and procalcitonin (PCT) concentrations on day 1 of the examination: Receiver Operating Characteristic (ROC) analysis.

ROC analysis of the presence or absence of symptoms on day 7 using serum Hp concentration, serum PCT concentration, and BRD score on day 1 of BRD examination (without symptoms on day 7: n = 15, with symptoms: n = 7).

AUC: area under the curve.

size, no clear trend of each marker by pathogen type was observed, and no statistical analysis was performed.

When evaluating the BRD score on days 2, 3 and 7, there were 7 calves that had a BRD score > 0, i.e., BRD symptoms persisted until day 7. Symptoms that persisted through day 7 were abnormal respiration in 5 calves (1 wheezing and 4 increased bronchial sounds), increased bronchial sounds and fever in 1 calf, and coarse crackles and fever in 1 calf. PCT on day 1 was positively correlated with BRD score on day 7 (r = 0.611, P = 0.00255). Hp and BRD score on day 1 were not significantly correlated with BRD score on day 7 (r = 0.218, P = 0.33; r = -0.00502, P = 0.982, respectively). To examine the relationship between the Hp, PCT, and BRD scores on day 1 and presence/absence of symptoms (BRD score ≥ 0) on day 7, the sensitivity and specificity of the Hp, PCT, and BRD scores were calculated and the Receiver Operating Characteristic (ROC) curves were visualized (Fig. 4). The area under the ROC curve (AUC), a measure of the predictive performance of the classification model, was 0.657, 0.824, and 0.543 for the Hp, PCT, and BRD scores, respectively. The cutoff values for serum PCT and Hp concentrations for predicting the presence of symptoms on day 7 of diagnosis were 17.8 pg/ml (sensitivity 0.867, specificity 0.857) and 435.8 μg/ml (sensitivity 0.533, specificity 0.857), respectively.

PCT is considered a specific biomarker for bacterial infections in humans[14,16,25]. Recent studies have measured PCT in calf blood[2,7,10], and the mean plasma PCT concentration in Holstein newborn calves was reported to be 33.3 pg/ml[7]. The average plasma Hp concentration in healthy Japanese black cattle was reported to be 0.1 μg/ml[30]. The serum PCT and Hp concentrations of healthy F1 fattening calves measured in this study were below the detection limit and 2.7 ± 0.2 μg/ml, respectively (Fig. 1); these low values were similar to the values previously reported. In contrast, both serum Hp and PCT concentrations in calves affected with BRD were significantly higher (Fig. 1). In this study, there was no clear relationship between serum PCT and Hp concentration (Fig. 1C). This may be because PCT and Hp have different induction mechanisms. The blood concentration of Hp, an acute phase protein, is increased by inflammatory cytokines (IL-6, TNF-α, IL-1β) that stimulate its synthesis and secretion[21,24]. PCT is secreted in response to stimulation by inflammatory cytokines TNF, IL-1β, IL-6, IL-8, and IL-10, and its expression is also induced by tissue damage[9]. The fact that PCT and Hp act relatively independently was also highlighted when their time course was evaluated (Fig. 2). Serum Hp was high on day 1, but significantly decreased on days 3 and 7

(Fig. 2). This was similar to a report of a decrease in Hp after treatment in BRD[32]. The serum Hp concentration on day 1 showed a negative correlation with the lymphocyte count on day 1 (Table 1). A decrease in lymphocytes due to acute inflammation caused by BRD has been reported[5], and it was speculated that the negative correlation between Hp and lymphocytes seen in this study reflected acute inflammation on day 1. However, the mean lymphocyte count on day 1 was within the normal range. A significant positive correlation was observed between Hp and rectal temperature on day 1 (Fig. 3A and Table 1). As Hp is known as a major acute phase protein in cattle, it was thought to reflect acute inflammation as well.

In contrast to Hp, persistently elevated levels of PCT were observed (Fig. 2). Sustained high PCT levels have been reported to be associated with poor prognosis in sepsis patients, indicating that PCT can be a useful prognostic biomarker in severe sepsis[4]. Furthermore, as a correlation was observed between the PCT value on day 1 and AST (Table 1), it is possible that calves with high PCT levels experienced BRD with lung tissue damage, and that respiratory abnormalities continued until day 7. The ROC analysis performed in this study showed that PCT had the best AUC value (Fig. 4), indicating an association between serum PCT concentration on day 1 and the presence of symptoms on day 7 (abnormal respiration). The ROC analysis results also imply that PCT values may reflect persistent disease, and it was thought to be superior to Hp in terms of prognosis prediction. These findings suggest that PCT measurement may be useful in the diagnosis and selection of treatment strategies for tissue damage (e.g., lung damage) that may cause persistent disease, particularly respiratory abnormalities.

A tendency to decreased serum albumin was observed in cattle with BRD (Table 1). Albumin is known to be a negative acute phase protein in cattle[19,24], and it was inferred that the decrease in albumin in this study reflected the inflammation of BRD. Respiratory rate, neutrophil count, monocyte count, and albumin/globulin were not associated with PCT and Hp on day 1 (Table 1). Increased respiratory rate was observed in BRD affected calves and was thought to be due to fever and decreased lung function[1]. Increased respiratory rate can also occur with heat, exercise, and acute stress[29], and increased respiratory rate in BRD has been reported to be unrelated to symptom severity[1]. Neutrophils have been reported to be increased in severe cases of BRD[1]. No association with neutrophil count was found in this study (Table 1) probably because there were no severe cases. Increased monocytes were observed during acute stress and during the healing phase of acute and chronic infections[26]. We have previously observed increased monocytes in BRD affected cows with elevated PCT[15], but not on day 1 of this study (Table 1). Albumin/globulin ratios have been reported to be decreased in BRD[18]. On the other hand, there are reports that albumin/globulin ratio did not decrease with some cases of BRD[6,18], and a decrease in albumin/globulin ratio is associated with BRD severity[18]. In the present study, it was within the reference value[12], presumably because there were no cases of severe BRD in this study.

The characteristics and differences between PCT and Hp demonstrated in this study suggest that measuring these markers can provide a multifaceted interpretation of the pathology of BRD-affected cattle. Further studies, including long-term follow-up of BRD chronic cases, investigation of more severe cases, and classification of the causative agent of BRD, will provide more detailed information on the usefulness of Hp and PCT as BRD biomarkers.

Acknowledgments

The authors thank the members of the Laboratory of Veterinary Hygiene for their helpful discussions.

Conflict of interest

The authors declare that they have no conflict of interest regarding the content of this manuscript.

References

1) Aktaş MS, Eren E, Aydın Ö, Yanar KE, Küçükler S, Eroğlu MS, Değirmençay Ş, İlgün M. Research on Hematology, Inflammatory and Antimicrobial Peptide Levels according to Clinical Scoring in Calves with Bovine Respiratory Disease (BRD). Van Veterinary Journal 35, 196–201, 2024. doi: 10.36483/vanvetj.1543947.
2) Akyüz E, Gökce G. Neopterin, procalcitonin, clinical biochemistry, and hematology in calves with neonatal sepsis. Trop Anim Health Prod 53, 354, 2021. doi: 10.1007/s11250-021-02779-z.
3) Aly SS, Love WJ, Williams DR, Lehenbauer TW, Van Eenennaam A, Drake C, Kass PH, Farver TB. Agreement between bovine respiratory disease scoring systems for pre-weaned dairy calves. Anim Health Res Rev 15, 148–150, 2014. doi: 10.1017/S1466252314000164.
4) Azevedo JRA de, Torres OJM, Czeczko NG, Tuon FF, Nassif PAN, Souza GD de. Procalcitonin as a prognostic biomarker of severe sepsis and septic shock. Rev Col Bras Cir 39, 456–461, 2012. doi: 10.1590/S0100-69912012000600003.
5) Baruch J, Cernicchiaro N, Cull CA, Lechtenberg KF, Nickell JS, Renter DG. Assessment of bovine respiratory disease progression in calves challenged with bovine herpesvirus 1 and Mannheimia haemolytica using point-of-care and laboratory-based blood leukocyte differential assays. Transl Anim Sci 5, txab200, 2021. doi: 10.1093/tas/txab200.
6) Bielamowicz LP, Celestino ML, Menta PR, Fernandes L, Ballou M, Neves RC, Machado VS. Association of Bovine Respiratory Disease during the Pre-Weaning Period with Blood Cell Counts and Circulating Concentration of Metabolites, Minerals, and Acute Phase Proteins in Dairy Calves Transported to a Calf Raising Facility. Animals (Basel) 14, 1909, 2024. doi: 10.3390/ani14131909.
7) Bonelli F, Meucci V, Divers TJ, Boccardo A, Pravettoni D, Meylan M, Belloli AG, Sgorbini M. Plasma procalcitonin concentration in healthy calves and those with septic systemic inflammatory response syndrome. Vet J 234, 61–65, 2018. doi: 10.1016/j.tvjl.2018.02.003.
8) Debra D M. Alterations in the leukogram. In: Large Animal Internal Medicine, 4th ed. Bradford PS. eds. Elsevier, St Louis. pp. 405-410, 2008.
9) Dong R, Wan B, Lin S, Wang M, Huang J, Wu Y, Wu Y, Zhang N, Zhu Y. Procalcitonin and Liver Disease: A Literature Review. J Clin Transl Hepatol 7, 51–55, 2019. doi: 10.14218/JCTH.2018.00012.
10) El-Deeb W, Elsohaby I, Fayez M, Mkrtchyan HV, El-Etriby D, ElGioushy M. Use of procalcitonin, neopterin, haptoglobin, serum amyloid A and proinflammatory cytokines in diagnosis and prognosis of bovine respiratory disease in feedlot calves under field conditions. Acta Trop 204, 105336, 2020. doi: 10.1016/j.actatropica.2020.105336.
11) Ercan N, Tuzcu N, Başbug O, Tuzcu M, Alim A. Diagnostic value of serum procalcitonin, neopterin, and gamma interferon in neonatal calves with septicemic colibacillosis. J Vet Diagn Invest 28, 180–183, 2016. doi: 10.1177/1040638715626488.
12) Gary PC. Clinical chemistry tests. In: Large Animal Internal Medicine, 4th ed. Bradford PS. eds. Elsevier, St Louis. pp. 375-397, 2008.
13) Hodgson PD, Aich P, Manuja A, Hokamp K, Roche FM, Brinkman FSL, Potter A, Babiuk LA, Griebel PJ. Effect of stress on viral-bacterial synergy in bovine respiratory disease: novel mechanisms to regulate inflammation. Comp Funct Genomics 6, 244–250, 2005. doi: 10.1002/cfg.474.
14) Jaresová M, Stríz I, Cermáková J, Lácha J, Sedlácek J, Mudra K, Hána I, Vítko S. Serum procalcitonin concentrations in transplant patients with acute rejection and bacterial infections. Immunol Lett 69, 355–358, 1999. doi: 10.1016/s0165-2478(99)00120-0.
15) Koshiishi T, Shibutani S, Chuma T, Iwata H. Measurement of serum procalcitonin concentrations in calves with bovine respiratory disease. Japanese Journal of

Veterinary Research 71, 65–71, 2023. doi: 10.57494/jjvr.71.2_65.

16) Linscheid P, Seboek D, Nylen ES, Langer I, Schlatter M, Becker KL, Keller U, Müller B. In vitro and in vivo calcitonin I gene expression in parenchymal cells: a novel product of human adipose tissue. Endocrinology 144, 5578–5584, 2003. doi: 10.1210/en.2003-0854.
17) Love WJ, Lehenbauer TW, Kass PH, Van Eenennaam AL, Aly SS. Development of a novel clinical scoring system for on-farm diagnosis of bovine respiratory disease in pre-weaned dairy calves. PeerJ 2, e238, 2014. doi: 10.7717/peerj.238.
18) Mahmoud AE, Fathy A, Ahmed EA, Ali AO, Abdelaal AM, El-Maghraby MM. Ultrasonographic diagnosis of clinical and subclinical bovine respiratory disease in Holstein calves. Vet World 15, 1932–1942, 2022. doi: 10.14202/vetworld.2022.1932-1942.
19) Marcato F, van den Brand H, Kemp B, van Reenen K. Evaluating Potential Biomarkers of Health and Performance in Veal Calves. Front Vet Sci 5, 133, 2018. doi: 10.3389/fvets.2018.00133.
20) Moisá SJ, Aly SS, Lehenbauer TW, Love WJ, Rossitto PV, Van Eenennaam AL, Trombetta SC, Bortoluzzi EM, Hulbert LE. Association of plasma haptoglobin concentration and other biomarkers with bovine respiratory disease status in pre-weaned dairy calves. J VET Diagn Invest 31, 40–46, 2019. doi: 10.1177/1040638718807242.
21) Murata H, Shimada N, Yoshioka M. Current research on acute phase proteins in veterinary diagnosis: an overview. Vet J 168, 28–40, 2004. doi: 10.1016/S1090-0233(03)00119-9.
22) Neumann S, Siegert S, Fischer A. Procalcitonin as an Endogenous Biomarker for Mastitis in Cows. Animals (Basel) 13, 2204, 2023. doi: 10.3390/ani13132204.
23) Pardon B, Hostens M, Duchateau L, Dewulf J, De Bleecker K, Deprez P. Impact of respiratory disease, diarrhea, otitis and arthritis on mortality and carcass traits in white veal calves. BMC Vet Res 9, 79, 2013. doi: 10.1186/1746-6148-9-79.
24) Petersen HH, Nielsen JP, Heegaard PMH. Application of acute phase protein measurements in veterinary clinical chemistry. Vet Res 35, 163–187, 2004. doi: 10.1051/vetres:2004002.
25) Principi N, Esposito S. Biomarkers in Pediatric Community-Acquired Pneumonia. Int J Mol Sci 18, 447, 2017. doi: 10.3390/ijms18020447.
26) Roland L, Drillich M, Iwersen M. Hematology as a diagnostic tool in bovine medicine. J Vet Diagn Invest 26, 592–598, 2014. doi: 10.1177/1040638714546490.
27) Ronald L T. Ruminant history, physical, examination, and records. In: Large Animal Internal Medicine, 4th ed. Bradford PS. eds. Elsevier, St Louis. pp. 3-14, 2008.
28) R Core Team. R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. http://wwwR-project.org/ 2024. [accessed on Aprill 16. 2024]
29) Trevisi E, Bertoni G. Some physiological and biochemical methods for acute and chronic stress evaluationin dairy cows. Italian Journal of Animal Science 8, 265–286, 2009. doi: 10.4081/ijas.2009.s1.265.
30) Tsukano K, Fukuda T, Ikeda K, Sato K, Suzuki K. Serum iron concentration is candidate inflammatory marker for respiratory diseases in beef cows. J Vet Med Sci 83, 824–828, 2021. doi: 10.1292/jvms.21-0051.
31) Windeyer MC, Leslie KE, Godden SM, Hodgins DC, Lissemore KD, LeBlanc SJ. Factors associated with morbidity, mortality, and growth of dairy heifer calves up to 3 months of age. Prev Vet Med 113, 231–240, 2014. doi: 10.1016/j.prevetmed.2013.10.019.
32) Wittum TE, Young CR, Stanker LH, Griffin DD, Perino LJ, Littledike ET. Haptoglobin response to clinical respiratory tract disease in feedlot cattle. Am J Vet Res 57, 646–649, 1996. doi: 10.2460/ajvr.1996.57.05.646.