Research Article

On-farm diagnosis of latent respiratory failure in calves

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Abstract: The goal of this study was to develop a method for the diagnosis of latent respiratory failure in calves with bovine respiratory disease (BRD) in farm conditions. The study involved 48 calves of the red-motley Holstein breed aged 14–28 days, with no previously experienced BRD, no dyspnea at rest, and a lack of anemia. Group I consisted of 24 calves with spontaneous or induced cough and WI clinical score of ≥5. Group II included 24 calves without spontaneous and induced cough and WI clinical score of ≤3. The determination of respiratory rate (RR), respiratory minute volume, and tidal volume in all calves was performed before and after functional exertion with a 15-min run and 30-s apnea. Blood samples were obtained from the jugular vein before 30-s apnea, then immediately after, and finally 1 min after apnea; blood gases and acid-base status were analyzed on an ABL-330, while total hemoglobin content was analyzed on a Micros-60. Tachypnea and dyspnea appeared after the 15-min run in group I calves, lasting 7.2 ± 0.4 and 3.7 ± 0.2 min. In group II calves, tachypnea lasted 3.8 ± 0.2 min, and no dyspnea occurred. Within 1 min, hypoxemia and hypercapnia caused by 30-s apnea in group II calves were compensated for due to an increase in pulmonary ventilation; in group I calves it was compensated for within more than 1 min, with presence of shallow breathing and dyspnea. The relation of RR immediately after 30-s apnea to RR before apnea showed excellent diagnostic value for detecting latent respiratory failure in the calves: area under the curve was 0.981, with cut-off point of ≥1.47, sensitivity of 95.8%, and specificity of 87.5%.

Key words: Calves, bovine respiratory disease, respiratory failure, dyspnea

1. Introduction

Bovine respiratory disease (BRD) remains a leading cause of illness, death, and decreased productivity for cattle around the world [1–3]. BRD in calves may involve the upper or lower respiratory tract [3,4]. Viral and bacterial infections of the upper respiratory tract such as rhinitis typically present with ocular and nasal discharge [1,3]. Infections of the lower tract, in contrast, may be challenging to detect earlier in the course of the disease [4]. In addition, the upper and lower respiratory tract infections may be different in severity. Necropsy and diagnostic testing for BRD pathogens is the gold standard test for diagnosing BRD in calves; however, such identification is not a routine practice unless BRD has become epidemic in a herd [3–5]. Imaging modalities, such as thoracic ultrasound and radiography, are also available to diagnose BRD ante mortem, but they rely on expensive equipment that requires specialized training to use and interpret [6–8]. Despite the variability of presentation, the observation of clinical signs remains the most common method used to identify calves in need of treatment for BRD [5].

One of the syndromes in calves with BRD is respiratory failure [9,10]. The term "respiratory failure" refers to the inability of external or internal respiration to provide blood with normal oxygen saturation and remove carbon dioxide, which is accompanied by weakness, cyanosis of the mucous membranes, and dyspnea [11–13]. Depending on the severity of dyspnea, there are three degrees of respiratory failure. First (latent) degree dyspnea occurs only with intense physical exertion; second degree dyspnea occurs with little exertion; third degree dyspnea is observed constantly both at rest and during physical exertion [12,14,15]. During respiratory failure of the first and second degrees, compensation of disturbances in gas exchange and oxygen deficiency in the blood are not observed [11,15]. Respiratory failure of the third degree is accompanied by hypoxia and/or hypercapnia, which can cause a coma and lead to the death of the animal [10–12].

In medicine, respiratory failure of the first and second degree is detected by applying dosed physical exertion and/or tests with a volitional breath inhibition during

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inhalation (Shtange test) and exhalation (Gench test). In case of respiratory failure, the time of volitional inhibition during inhalation is less than 30 s, and on exhalation it is less than 20 s [14,15].

In veterinary medicine, the methods for diagnosis of respiratory failure are described mainly in horses [16–18]. Only a few studies [9,10,19] are devoted to the diagnosis of respiratory failure in calves. The development of methods for diagnosing latent respiratory failure in calves in farm conditions may be useful not only for identifying and controlling BRD but also for the selection and rejection of animals for sale as well as group formation. The purpose of this study was to develop a method for diagnosis of latent respiratory failure in calves with BRD in farm conditions.

2. Materials and methods

2.1. Animal materials and study design
The research was performed during winter, when the cattle were kept in stalls, on a farm impacted by BRD (*Mycoplasma bovis* and bovine viral diarrhea virus 1). It included 48 calves of the red-motley Holstein breed, ages ranging from 14 to 28 days, with a body weight range of 48–57 kg. All calves were subjected to functional exertion: running for 15 min and then, following a 2-h resting period, a 30-s artificial respiration inhibition (apnea) upon exhalation. The type, rhythm, and frequency of breathing per minute before and after the functional exertion, as well as breath recovery time after the exertion, were taken into account. The ratio of respiration frequency during the minute after exertion to the respiration frequency during a minute at rest was calculated. Using an SSP spirometer (KPO Medaparatura, Ukraine) and a mask with a valve system that was fixed onto the calves, we determined respiration frequency, respiratory minute volume, and tidal volume at rest after 30 s of apnea. Calves were evaluated using the WI clinical scoring system that was developed by veterinarians at the University of Wisconsin at Madison [20]. Samples of venous blood that were used for laboratory studies were obtained immediately before apnea, immediately after apnea, and 1 min after apnea in all calves. Group I included calves that met the following criteria: 1) absence of previously contracted BRDs; 2) no dyspnea at rest; 3) lack of anemia; 4) the presence of spontaneous or induced cough; 5) score on the WI system of ≥5 points. Criteria for inclusion of calves in group II were: 1) absence of previously contracted BRD; 2) no dyspnea at rest; 3) lack of anemia; 4) lack of spontaneous or induced cough; 5) score on the WI system of ≤3 points.

2.2. Collection of samples
Blood samples from calves were obtained anaerobically from a jugular vein catheter (1.8 × 45 mm, M. Schilling GmbH, Germany) and collected into sterile vacuum tubes with EDTA. All blood samples were subjected to laboratory testing 5–10 min upon receipt.

2.3. Determination of hemoglobin
Total hemoglobin content in blood was determined using the Micros-60 analyzer (Horiba ABX, France).

2.4. Analysis of blood gases and acid-base status
pH, partial pressure of carbon dioxide (pCO_2) and oxygen (pO_2), concentration of carbonic acid (H_2CO_3), actual bicarbonates (AB), sums of bicarbonates (buffer bases, BB), and excess or deficiency of buffer bases (BE) in venous blood were examined using the ABL-330 automatic blood gas analyzer (Radiometer, Denmark). pO_2 was measured by the amperometric method, pH and pCO_2 were measured by direct potentiometry, and other indicators were calculated [21,22]. The results of pH and pCO_2 measurements were related to the Nernst equation potential. pH, pCO_2, and pO_2 values, obtained at a temperature different than 37 °C body temperature, were corrected by introducing the body temperature of the animal in the corresponding field on the analyzer monitor [21,22].

2.5. Statistical analysis
For statistical analysis, the independent sample t-test was used to determine the difference between groups I and II. Statistical evaluations of differences between calves before apnea, immediately after apnea, and 1 min after apnea were done by using the paired t-test in STATISTICA 8.0 (StatSoft Inc., USA). Statistical significance was set at P < 0.05. All datasets were expressed as mean ± standard error of the mean (SEM). The diagnostic cut-off point of the analyzed indicators of respiratory failure in calves was determined using ROC analysis in IBM SPSS Statistics 20.0 (IBM Corp., USA) according to the method of DeLong et al. [23]. The following ROC curve parameters were analyzed: area under the curve (AUC), sensitivity (%), specificity (%), and cut-off point.

3. Results
The metrics that characterize the response of calves to functional exertion (running for 15 min) are presented in Table 1. After the 15-min run, the calves of group I had increased their respiration rate by 73.1% (P < 0.01) and returned to their initial values in 7.2 ± 0.4 min. In the run of 8–10 min, the animals had to be physically urged to move. All of the calves in group I had severe dyspnea after the run, which lasted from 2.6 to 5.1 min, and 91.7% of the animals had a cough. In the calves in group II, after a 15-min run, the respiration rate increased by 59.7% (P < 0.01) and returned to baseline values in 3.8 ± 0.2 min, which is 47.2% (P < 0.05) less than in group I; no dyspnea was observed.

The changes in pulmonary ventilation metrics in the calves after physiological exertion (30 s of apnea) are shown in Table 2. After 30 s of apnea all calves in group I had a cough and dyspnea. The manifestation of anxiety was

Table 1. Reaction of calves to functional exertion – running for 15 min.

Parameter	Group I (n = 24) Mean ± SEM	Group II (n = 24) Mean ± SEM
Respiratory rate per minute at rest (baseline values)	28.3 ± 0.7	24.8 ± 0.6
Respiratory rate per minute after 15-min run	49.0 ± 0.8	39.6 ± 0.4
The return time of respiratory rate to baseline values, min	7.2 ± 0.4[a]	3.8 ± 0.2
Dyspnea duration, min	3.7 ± 0.2[b]	0
Calves with a cough reaction to the run, n (%)	22 (91.7)	0 (0)

Statistical importance between group I and group II: [a] $P < 0.05$, [b] $P < 0.01$.

Table 2. Parameters of pulmonary ventilation in calves before and after 30-s apnea.

Parameter	Group I (n = 24) Mean ± SEM			Group II (n = 24) Mean ± SEM		
	Before apnea	After apnea	P	Before apnea	After apnea	P
Respiratory rate per minute	28.4 ± 0.6	57.9 ± 3.3	**	24.3 ± 0.7	32.1 ± 2.5	*
Respiratory min volume, L	12.8 ± 0.4	27.3 ± 1.2	***	12.2 ± 0.6	22.3 ± 0.5	**
Tidal volume, mL	458.0 ± 10.0	423.5 ± 3.8	NS	496.3 ± 9.8	768.3 ± 28.9	**

* $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$, NS: not significant.

common in calves within 15–25 s of apnea. In the animals of group I, after apnea, the respiratory rate and respiratory minute volume increased by 103.9% (P < 0.01) and 113.3% (P < 0.001), respectively, compared with baseline values before apnea, while tidal volume had no significant change. Respiratory rates after apnea returned to the baseline values observed before apnea within 2–5 min. The ratio of the respiratory rate after apnea to the initial respiratory rate before apnea observed in group I calves ranged from 1.43 to 3.89, with an average of 2.24 ± 0.15.

Apnea for 30 s did not cause anxiety, dyspnea, or a cough in the calves of group II. The respiratory minute volume and tidal volume observed after apnea increased by 82.8% (P < 0.01) and 54.8% (P < 0.01), respectively, compared with baseline values before apnea. Per minute respiratory rate observed after apnea increased by 32.1% compared with the level before apnea (P < 0.05) and returned to baseline values within 1–2 min. The ratio of respiratory rate after apnea to respiratory rate before apnea in calves of group II ranged from 1.07 to 1.68, with an average of 1.29 ± 0.03.

Changes in the gas composition of the calves' venous blood after apnea are shown in Figures 1 and 2. In the animals of group I, the partial pressure of carbon dioxide in blood pCO_2 after 30 s of apnea increased by 22.6% (P < 0.01) as compared to the initial level before apnea, and it did not change after 1 min. At the same time, after apnea, the partial pressure of oxygen pO_2 in the blood decreased

by 38.9% (P < 0.01) and 1 min after apnea it remained 27.8% (P < 0.05) lower than the initial values. In the calves of group II, 30 s of apnea did not cause significant changes in the gas composition of venous blood; pCO_2 and pO_2 returned to their original values 1 min after apnea.

The acid-base status of calves is shown in Table 3. In 45.8% of the calves in group I, the acid-base status was characterized as partially compensated metabolic alkalosis; in 54.2% it was characterized as decompensated respiratory metabolic acidosis. A significant increase in the concentration of topical AB bicarbonates and BE buffer bases in venous blood in the calves with partially compensated metabolic alkalosis could not be fully compensated by carbon dioxide elimination, which led to an increase in blood pH. With decompensated respiratory metabolic acidosis in the calf blood, there was a significant increase in the partial pressure of carbon dioxide pCO_2 and a deficiency in buffer bases of BE in calves, which led to a decrease in blood pH.

In 75.0% of calves in group II, the acid-base status was characterized as compensated respiratory alkalosis; in 25.0% it was characterized as compensated metabolic acidosis. The partial pressure of oxygen pO_2 in the blood was at the optimal level.

ROC analysis showed an excellent diagnostic value (AUC = 0.981) of the "ratio of respiratory rate per minute after 30-s apnea to respiration rate per minute at rest
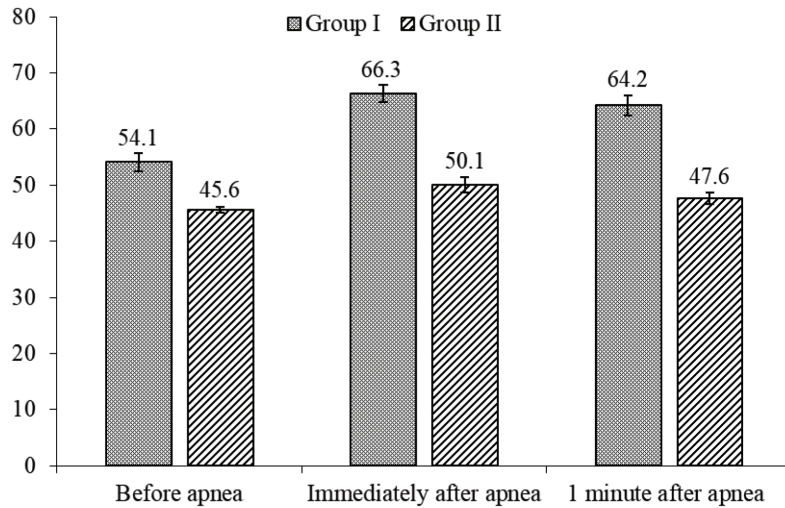
Figure 1. Partial carbon dioxide pressure (pCO_2) in venous blood of calves before apnea, immediately after, and 1 min after apnea, mmHg.
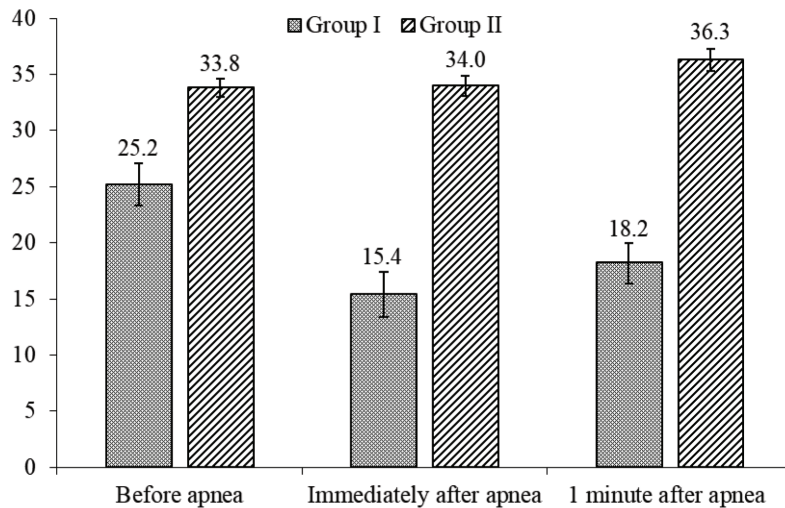

Figure 2. Partial oxygen pressure (pO_2) in venous blood in calves before apnea, immediately after, and 1 min after apnea, mmHg.

before apnea" in order to identify latent respiratory failure in calves. We designated this indicator as the "respiratory failure index" (RFI). For the RFI cut-off point of ≥1.47, the sensitivity was 95.8% and the specificity was 87.5%.

4. Discussion
Respiratory diseases are among the most common diseases in young cattle [1–3]. In the Russian Federation, the incidence of BRD among calves aged 14–28 days varies from 17.0% to 86.6% [3]. The mortality from respiratory diseases, reduction of growth rates, and preventive and therapeutic measures are some of the reasons for significant economic losses [24]. Respiratory dysfunction in calves is proven to be associated with a wide range of pathological

findings in lung parenchyma and in respiratory tracts [1,3,4]. Frequently, it is difficult to assess the degree of lung tissue damage solely through clinical examination, which may result in treatment delay and a questionable prognosis [3–7]. At the same time, clinical manifestation differs quite often; the diagnosis should identify the location, severity, and intensity of lung tissue damage in respiratory disease course [7,25]. To expand the possibilities of diagnosing the respiratory tract in calves, the method of functional diagnosis of the lungs is applied [3,26].

Both in human medicine and in veterinary medicine, dosed exercise is the most commonly used method for detecting respiratory failure in patients. In first degree respiratory failure (latent), shortness of breath appears

only after intense physical exertion; in second degree respiratory failure, shortness of breath occurs after even a small activity; in third degree respiratory failure, shortness of breath is observed constantly, both at rest and during physical exertion [12,14,15].

It is known that in trained healthy trotting horses the respiration rate increases up to 20–24 per minute after a 15-min trot run and is restored to the initial level in 7–10 min. In poorly trained horses, respiration rate increases to 28–34 per minute and is restored only 12–15 min after the run; an increase in the frequency of respiration up to 45 per minute or more is observed in horses with cardiac and/or respiratory failure. Restoration of respiration rate comes to baseline values in such animals with a great delay, 20–30 min or more after exercise [18].

The current findings showed that a 15-min run allowed the detection of latent respiratory failure in calves, but it was hard to bear by the animals. After 8–10 min of running, the calves of group I had to be forced to move. The data presented in Table 1 show that in the calves of group I, severe dyspnea appeared after the run, which lasted from 2.6 to 5.1 min; the respiration rate also increased by 73.1% (P < 0.01) and returned to baseline values in 7.2 ± 0.4 min, which was 89.5% (P < 0.05) longer compared to the animals of group II.

In human patients, samples with a volitional breath hold on inhalation (Shtange test) and exhalation (Gench test) are also used to identify respiratory failure of the first and second degree [14,15]. As an alternative to these tests, a 30-s artificial breathing inhibition (apnea) upon exhalation was used in the present work for the first time to diagnose latent respiratory failure in calves.

The data presented in Table 2 show that the reactions to 30-s apnea in calves in groups I and II differed significantly. In group II animals, 30-s apnea caused an increase in both the respiratory rate per minute by 32.1% (P < 0.05) and tidal volume by 54.8% (P < 0.01), resulting in a respiratory minute volume increase by 82.8% (P < 0.01) compared with baseline (before apnea). In the calves in group I, a compensatory increase in respiratory minute volume by 113.3% (P < 0.001) after apnea occurred only due to an increase in the respiratory rate per minute (by 103.9%, P < 0.01), while the tidal volume in comparison with the initial level (before apnea) did not change. The ratio of respiratory rate per minute after apnea to respiratory rate per minute before apnea in calves in group I was 73.6% (P < 0.05) higher than in animals in group II.

A research method such as blood gas analysis fully assesses metabolic and respiratory acid-base problems both qualitatively and quantitatively, including the correlation between ventilation, oxygenation, and metabolism in animals with respiratory failure, enabling specialists to choose the correct therapy approach. This can be used to track trends in animals and to understand the severity of the disease [24,27].

Figures 1 and 2 illustrate that in calves, 30 s of artificial breathing inhibition (apnea) upon exhalation led to oxygen deficiency as well as an increase in carbon dioxide content in the blood. However, in animals in group II the content of oxygen and carbon dioxide in venous blood returned to baseline values within 1 min after apnea. In calves in group I, pCO_2 remained 18.7% (P < 0.05) higher in blood 1 min after apnea, and pO_2 was 27.8% lower (P < 0.05) compared to baseline values, indicating that they had respiratory failure [9–11].

During respiratory failure, the lungs are not able to provide blood with normal oxygen saturation and carbon dioxide excretion; therefore, any exertion (apnea or running) leads to an accumulation of carbon dioxide, a reduction of blood oxygen saturation, and, consequently, increased frequency of respiration, dyspnea, and increased respiratory rate as compared to initial values. The more time it takes to restore breathing to its initial values after exertion, the more pronounced the respiratory failure.

The present study shows that both methods—a 15-min run and 30-s apnea—can be used to diagnose latent respiratory failure in calves. In healthy calves, the time for respiratory movements to return to baseline values after a 15-min run does not exceed 4.8 min, and with latent respiratory failure, it is 4.9–10.5 min or more. However, the use of a 15-min run to detect latent respiratory failure in calves while in farm conditions is very time-consuming and can cause anxiety in animals located in neighboring machines. The preferred method for diagnosing latent respiratory failure in calves under farm conditions is to determine the respiratory rate per minute at rest and then after 30 s of apnea with a subsequent calculation of the ratio of respiratory rate after apnea to the initial respiratory rate before apnea, which we called RFI. The results of the ROC curve analysis revealed the excellent diagnostic value of this indicator: AUC was 0.981 for the RFI cut-off point of ≥1.47, sensitivity was 95.8%, and specificity was 87.5%, with normal values ranging from 1.07 to 1.46. In calves with latent respiratory failure, the RFI was 1.47 or higher.

Respiratory failure is not considered a disease, but a dysfunction resulting from the problems affecting the ability to breathe [11–15]. The term refers to a syndrome in which the respiratory system fails in one or both of its gas exchange functions: oxygenation and carbon dioxide elimination. In most cases, respiratory failure initially affects the ability to either absorb oxygen (oxygenation failure) or eliminate carbon dioxide (ventilatory failure) [11].

In the pathogenesis of respiratory diseases in calves, ventilation problems, pulmonary diffusion, pulmonary hemodynamics, and/or inadequate ventilation-perfusion

Table 3. Blood gases and acid-base status of calves.

Parameter	Group I (n = 24) Mean ± SEM		Group II (n = 24) Mean ± SEM	
Acid-base status	Partially compensated metabolic alkalosis (n = 11)	Decompensated respiratory metabolic acidosis (n = 13)	Compensated respiratory alkalosis (n = 18)	Compensated metabolic acidosis (n = 6)
pH	7.43 ± 0.01	7.24 ± 0.01	7.35 ± 0.05	7.31 ± 0.02
pCO_2, mm Hg	54.1 ± 0.4	54.0 ± 0.2	42.2 ± 0.8	41.1 ± 0.2
pO_2, mm Hg	25.2 ± 1.4	20.3 ± 0.3	37.2 ± 0.4	35.7 ± 0.4
AB, mmol/L	33.9 ± 0.8	23.1 ± 0.4	23.9 ± 0.2	20.1 ± 0.5
BE, mmol/L	+9.2 ± 0.8	−5.7 ± 0.2	−1.9 ± 0.4	−6.5 ± 0.3
H_2CO_3, mmol/L	1.62 ± 0.01	1.63 ± 0.04	1.28 ± 0.02	1.23 ± 0.04
AB/H_2CO_3	22.3 ± 0.9: 1	13.3 ± 0.6: 1	19.0 ± 0.4: 1	16.4 ± 0.6: 1
BB, mmol/L	51.2 ± 0.9	36.1 ± 0.1	40.3 ± 0.1	35.6 ± 0.2

state can lead to a decrease in the level of oxygen in arterial blood. Respiratory acidosis can result from an increase in pCO_2, often observed with respiratory disorders or with impaired respiratory distribution. Due to the compensatory manifestations of the respiratory (hyperventilation) and circulatory system (increase in heart rate and minute volume), it is possible to maintain an adequate overall oxygen consumption, despite respiratory failure, shortly before death [28]. Hypoxic pulmonary vasoconstriction is a regulatory mechanism in alveolar hypoventilation by which blood flow results from alveolar hypoventilation and hypoxia and is diverted from poorly ventilated areas to better ventilated alveolar regions. This system is to improve the ventilation/perfusion ratio in case of atelectasis. Although the blood redistribution mechanism described is useful in the case of localized alveolar hypoxia, it can have serious consequences for the functioning of the right heart in generalized hypoxia, for example, in animals with severe diffuse lung diseases [29].

Our study found a significant decrease in pO_2 and an increase in pCO_2 values by 15.7% and 34.1% ($P < 0.05$), respectively, in venous blood in calves with respiratory failure (group I) compared to healthy animals (group II). Šoltésová et al. [30] described the highly correlated severity of respiratory diseases and the values of oxygen partial pressure and hemoglobin oxygen saturation. Changes that were noted in calves with the disease were compared with the clinical picture, reducing the values even in mild cases. About half of the calves with severe respiratory syndrome had indicators of partial pressure of oxygen and saturation of hemoglobin with oxygen common to venous blood. Meanwhile, an increase in pCO_2 values was reported only in calves with severe clinical symptoms [30]. Calves with severe clinical symptoms of BRD were not included in our

study. The clinical assessment of the WI system in calves of group II was from 5 to 8, with an average of 5.95 ± 0.27. At the same time, some authors reported that in calves suffering from clinically undifferentiated bronchopneumonia, a decrease in pO_2 values occurs together with an increase in pCO_2 [26,31]. Similar to our work, for example, other authors recorded a noticeable decrease in pO_2 values and pCO_2 values in calves with chronic bronchopneumonia, slightly lower than in healthy animals [32]. A higher respiratory rate and hyperventilation may explain lower pCO_2 values. Such a direction of similar alterations in the above-mentioned indicators was observed in calves suffering from certain respiratory diseases, such as infection, bovine respiratory syncytial virus [33,34], bovine herpesvirus [9], verminous bronchopneumonia [35], or pneumonia induced by *Pasteurella haemolytica* [10,36,37]. Hypoxia and elevated pCO_2 values were recorded in all cases due to extensive damage to the lung parenchyma with atelectasis upon death, exudative pneumonia, and obstructive purulent bronchiolitis [36]. Despite the fact that pO_2 is not associated with the clinical picture in all cases, it is an important indicator of lung diffusion capacity dysfunction, thus confirming the degree of lung damage, and is considered to be reliable enough in severity of damage [38,39]. Diffusion and gas distribution disorders are assumed to be among the main reasons for hypoxemia [33,40]. In addition, the pronounced clinical signs of BRD, decreasing pO_2 with increasing pCO_2 in animals' arterial blood, indicate obstructive changes and ventilation disorders [41]. For their part, obstructive respiratory disorders can cause an uneven distribution of ventilation and inconsistency between the ventilation and perfusion system with hypoxemia, hypoxic vasoconstriction, and pulmonary vascular hypertension, and in more severe cases of hypercapnia [42].

According to Šoltésová et al. [30], most calves with higher pCO_2 values were identified to have compensated respiratory acidosis due to respiratory diseases. Lower blood pH values in calves suffering from bronchopneumonia in contrast to healthy ones were also reported by Vestweber et al. [32]. The results of our research show that the main disorders of acid-base states that accompany respiratory failure in calves with BRD (group I) are characterized as partially compensated metabolic alkalosis (45.8%) and decompensated respiratory metabolic acidosis (54.2%). In the meantime, the acid-base states in healthy calves (group II) are characterized as compensated respiratory alkalosis (75.0%) or compensated metabolic acidosis (25.0%), as is evident from the data in Table 3. With compensated respiratory alkalosis in calves, a slight initial decrease in pCO_2 in venous blood is compensated by a decrease in BE concentration, as a result of which the pH of the blood remains within normal range [43,44]. The partial pressure of oxygen in the blood is at the optimal level. In compensated metabolic acidosis, the primary deficiency of AB and BE in the blood is compensated by a decrease in pCO_2, keeping the pH value in the optimal range; pO_2 in the blood is within normal range [43,44].

In previous research [45] we showed that when other symptoms of BRD were missing, acid-base states in 66.7% of calves with induced cough were characterized as respiratory-metabolic acidosis, compensated or decompensated. The other 33.3% were characterized as compensated respiratory acidosis; there was a significant decrease in pO_2 and an increase in pCO_2 values in the blood. At the height of BRD, among all disturbances of acid-base balance in calves, metabolic alkalosis was dominant, seen to be compensated, partially compensated, and decompensated in 25.0%, 66.7%, and 8.3% of animals, respectively; there was a significant increase in pCO_2 without a change in pO_2 value in the blood [45]. Thus, the acid-base status in calves with BRD can vary significantly depending on the phase and severity of the disease. Respiratory failure indices extend not only to the respiratory system but also trigger the acid-base balance in general, which is fully confirmed by research results.

In conclusion, functional tests—a 15-min run and 30-s apnea—increase the ability to identify calves with latent forms of BRD in a farm setting. In respiratory failure in calves, the lungs are unable to provide the blood with normal oxygen saturation and carbon dioxide emissions, so any tension (apnea or running) leads to the accumulation of carbon dioxide and a decrease in blood oxygen saturation. This is manifested by an increase in respiratory rate per minute and dyspnea. The longer it takes for calves to restore breathing after exercise to their initial values at rest, the more manifested is the respiratory failure. In calves with respiratory failure, the resumption time of respiratory rate after exercise to initial values (at rest) is 4.9–10.5 min or more; in healthy animals it does not exceed 4.8 min. As an alternative to the Shtange and Gench tests used to diagnose latent respiratory failure in humans, in calves, 30-s exhalation apnea can be applied. Lack of oxygen and an increase in carbon dioxide content in the blood caused by 30-s apnea in healthy calves are compensated for by an increase in pulmonary ventilation and return to initial values within 1 min. In calves with latent respiratory failure, after 30 s of apnea the tidal volume does not drastically change, but there is a significant increase in respiratory rate per minute, breathing becomes shallow, dyspnea appears, and the respiratory rhythm is restored within 2–5 min. The high diagnostic value (sensitivity: 95.8%, specificity: 87.5%) for detecting latent respiratory failure in calves was shown by the definition of the RIF, calculated as the ratio of the respiratory rate per minute after 30 s of apnea to the respiratory rate per minute before apnea (at rest). In calves with latent respiratory failure, RFI was 1.47 or more; in healthy animals it ranged from 1.07 to 1.46. Application of 30-s apnea and the RFI can be an appropriate tool for diagnosing latent respiratory failure in calves in farms since it does not require special skills or expensive equipment use.

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