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The impact of environmental factors on bovine respiratory disease complex in dairy calves - a review

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Abstract

Bovine respiratory disease complex (BRDC) is a multifactorial disease in which, in addition to infectious agents and the individual resistance of animals, technological, management and climatic factors also play a role. Outdoor rearing in small groups has many advantages in terms of BRDC prevention. Continuous real-time monitoring of environmental factors, such as the temperature, relative humidity, air velocity, bioaerosols and harmful gases can also help to prevent damage by BRDC. Low temperatures in combination with elevated relative humidity and windspeed can lead to increased morbidity and mortality. Among noxious gases, ammonia may be of the greatest importance for respiratory diseases, as it directly damages the respiratory tract, leaving room and opening gate for pathogenic and opportunistic microbes. Bioaerosols of livestock buildings consist of feed, manure, organic matter from animals (e.g., epithelial cells, hair, urine, faeces), microorganisms, and toxins. Due to their size, particulate matter (PM) particles (PM10 and PM2.5) have important health effects, leading to severe respiratory and systemic diseases. Particulate matter formation and concentration depend on the housing and feeding conditions, species housed, stocking density, animal activity and environmental factors, but also on the sampling periods within a day. High temperature, low humidity, air movement (especially drafts), and increased activity of animals also cause the manure to dry, leading to dust formation and particles becoming airborne. With increased environmental control, the effects of the climatic factors on the calves health can be more easily identified, measures can be taken to reduce them, thus the occurrence and damage of possible diseases (mainly respiratory, BRDC) can be decreased.

Particulate matter, ammonia, wind speed, humidity, BRDC

One of the most common causes of dairy industry losses is the bovine respiratory disease complex (BRDC) (Gorden and Plummer 2010; Panciera and Confer 2010), which is attributable to multifactorial causes, such as infectious agents, individual resistance, climatic, husbandry, and management factors (Gulliksen et al. 2009b; Griffin et al. 2010; Ózsvári and Búza 2015; Buczinski et al. 2018b; Stokstad et al. 2020). Clinical cases are usually only the tip of the iceberg and a much higher proportion of lung lesions can be found at slaughter (Timsit et al. 2016; Stokstad et al. 2020). In a Czech study, acute pathological lung findings were determined in 9.22% of calves, whereas chronic pathological lung findings were determined in 35.63% of calves during carcass inspection (Kaluza et al 2021). The economic losses of acute illnesses can be inferred from the costs of treatments and deaths. Indirect damages include reduced feed conversion and weight gain (Guterbock 2014; Stokstad et al. 2020), extended first insemination and calving date (Ózsvári et al. 2012; Ózsvári and Búza 2015), and losses due to lower first lactation milk production (Dunn et al. 2018).

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In 90% of cases, the primary infectious agents are viruses, the most significant being BRSV, PI-3, BHV-1, BVDV and BCoV (O'Neill et al. 2014). Depending on the susceptibility of the host and the heterogenity between virus strains (Mosier 2014), they can cause disease directly, or contribute to the development of secondary bacterial infections, mainly attributable to *Mannheimia haemolytica*, *Pasteurella multocida*, *Histophilus somni*, and *Mycoplasma bovis* (Lorenz et al. 2011). They proliferate under stress and colonize the lower respiratory tract; moreover, direct tissue damage is enhanced by their virulence factors (encapsulation, adhesins, toxins, enzymes, biofilm). This elicits an intense inflammatory response and even promotes their synergistic effect, leading to even more serious illnesses (Panciera and Confer 2010; Taylor et al. 2010; Mosier 2014). Although these pathogens can be isolated from the airways of calves showing symptoms of BRDC, experimental infection has failed to reproduce the typical symptoms of BRDC (Jericho and Langford 1978). Moreover, such pathogens can be isolated from the airways of healthy cattle as well (Allen et al. 1992; Fulton et al. 2002) and field conditions can not be fully reproduced during experiments (Philippe-Reversat et al 2017). All this suggests that individual resistance and various predisposing factors are also important in the development of BRDC. Control programs can eradicate IBR and BVDV from herds: Scandinavian countries, Switzerland, Germany, some Italian Provinces and Czech Republic are already IBR-free, whereas Slovakia, Hungary, Poland and Ukraine run IBR control programs (Mandelik et al 2021).

Cattle are more prone to pneumonia due to their anatomical, physiological, and immunological properties, such as high respiratory dead space volume and poor collateral ventilation, pulmonary intravascular macrophages and circulating gamma-delta T-cells. Although respiratory dead space volume alone does not necessarily impair airway defenses, it provides a large surface for the deposition of airborne dust particles and can also increase the transit time of inhaled gases and dust (Ackermann et al. 2010). It is believed that inherited resistance could be enhanced by targeting genetic resistance (Mosier 2014).

Some environmental and management factors contribute to the development of BRDC by facilitating the spread and survival of pathogens and weakening the overall defense mechanism resistance of the calves' respiratory system by causing increased stress (Ackermann et al. 2010). Main risk factors are group housing and large group size, poor bedding, direct contact with older animals, unfavourable climatic conditions (heat, cold, snow, frost) and inadequate air quality such as high humidity, dust, harmful gases (Lundborg et al. 2005; Lago et al. 2006; Svensson and Liberg 2006; Taylor et al. 2010; Ózsvári and Búza 2015). Herd size may also have some effect, as in larger herds stockmen tend to have lower awareness of and spend less time attending to the animals (Slavík et al. 2009).

Housing types

Environmental factors influence the incidence and severity of diseases (Gulliksen et al. 2009b), and so we aim to mitigate their effects when designing housing conditions (Roland et al. 2016) with particular regard to ambient temperature and humidity due to their effect on thermoregulation and production (Seedorf et al. 1998).

As early as the 1950s, the benefits of outdoor individual calf rearing compared to indoor group housing were studied: higher weight gain, less diarrhoeal diseases, and a negligible number of respiratory problems were expected for individual rearing (Davis et al. 1954). The outdoor calf hutch is beneficial for the prevention of respiratory and other diseases, as it facilitates free movement of air and low concentration of pathogens in the open air; moreover, the cages can be placed at appropriate distances to reduce contact between calves (Callan and Garry 2002; Gorden and Plummer 2010; Malá and Novák 2021), thereby decreasing morbidity and mortality. However, not only the basic needs of calves need to be met when choosing a technological housing system; suitable working conditions for farm staff need to be considered, as well (Malá and Novák 2021), since caretaking is difficult in adverse weather conditions (Lorenz et al. 2011). In order to enhance the comfort of workers and reduce the exposure of calves to cold stress, barn rearing is also popular, although efforts are often made to maximize the number of calves kept indoors (Nordlund 2008; Gorden and Plummer 2010), which can be unfavourable in terms of airborne diseases (Islam et al. 2020). The ideal individual calf cage set up in a barn is at least 3 m^2 in size, with solid walls on both sides, nets at the ends, and deep straw litter (Lago et al. 2006). The use of solid walls reduces the exchange of pathogens between the individual cages and thus the prevalence of respiratory diseases and avoids direct contact between calves (Nordlund 2008). However, the microclimate of such calf cages may differ significantly from the central part of the barn (Lorenz et al. 2011). This can lead to the development of a highly polluted microenvironment in an otherwise well-ventilated barn (Nordlund 2008), and increases the aerial germ load, which is related to the incidence of respiratory diseases (Lago et al. 2006). Individual outdoor hutches have been associated with lower morbidity and mortality in dairy calves and have better subsequent production and reproduction compared to calves kept in individual pens under shelter (Malá and Novák 2021). Individual hutches can be made from different materials with different advantages and disadvantages. In terms of the microclimate, wooden hutches have better climate in summer, whereas tarpaulin, fiberglass or polyethylene hutches may get overheated when there is a lack of ventilation holes (Malá and Novák 2021). In the European Union, solid walls cannot be used during calf rearing and individual rearing is only permitted until the age of 8 weeks because of space requirements and social behaviour (European Council 2009).

The microclimatic conditions of naturally ventilated barns correlate with the outdoor temperature and a seasonal pattern can also be observed (Seedorf et al. 1998). The microclimate of the barn is affected by a number of factors such as the temperature of the air and the barn surfaces, humidity, wind speed, concentration of harmful gases, dust and microbes (Roland et al. 2016). As stocking density increases, the barn temperature increases linearly (Cooper et al. 1998). At lower stocking densities, the difference between indoor and outdoor temperatures decreases, and differences in temperature between barn sections with different stocking densities can be observed as well (Wagner-Storch and Palmer 2002).

Small group housing

Group housing is becoming increasingly popular in terms of health and animal welfare (Roland et al. 2016). It requires significantly less labour and, in some cases, can be mechanized well. Outdoor group housing can combine the benefits of individual cage housing and group rearing (Nilsson 2012; Wójcik et al. 2013b), as outdoor housing provides better air quality and hygiene, lower mortality, higher feed consumption and growth rate compared to indoor housing; however, a draft-free microclimate and adequate bedding must be ensured outdoor as well (Roland et al. 2016). In a German experiment (Wójcik et al. 2013a), calves housed in igloos in groups of 15 from 3 weeks up to 3.5 months of age had significantly higher body weight and daily weight gain, while the number and proportion of sick days and mortality were lower compared to group-housed calves in barns. In a Polish experiment in calves (between days 5 and 90 of age) were raised in indoor group pens (5 calves/pen) and in individual outdoor hutches. During the first month, there were no differences between daily gains of groups. Later, the calves raised indoors were characterised by better daily gains, feed intake and as a result, body weight, meanwhile the outdoor system had a positive effect on morbidity, mainly in terms of pneumonia and diarrhoea (Wójcik et al. 2013b). According to a Swedish study (Nilsson 2012), the number of respiratory illnesses was reduced by almost a half, but the incidence of diarrhoea has also fallen, and all antibiotic use was nearly halved after switching from traditional indoor group housing to outdoor group housing. The benefits of igloo-like outdoor hutches are evident not only in temperate but also in extremely dry environments (Razzaque et al. 2009).

Groups can be formed in a stable, all-in-all-out system, which consists of calves of the same age. When the group is relocated, the calf house is cleaned and disinfected before new calves are resettled. In dynamic systems, the group size is constant with older calves being constantly replaced by young individuals, so the calf house is cleaned and disinfected only every few months. Respiratory and diarrhoeal diseases were more than twice as common in dynamic groups (6-6 calves) than in stable groups (Pedersen et al. 2009). Several recommendations have been given for the group size, with some suggesting 6 to 10 calves (Svensson and Liberg 2006; Bach and Ahedo 2008; Babu et al. 2009), and other sources preferring smaller groups of 2 to 6 (Losinger and Heinrichs 1997). The all-in-all-out system is recommended. For example, a Norwegian survey found that respiratory disease was 3.9 times more common in groups where the age difference between calves was more than 8 weeks (Gulliksen et al. 2009b). Examining small-group (8 calves) calf houses, in groups of 2 or 3 calves that were asymptomatic at the time of grouping but had BRDC before weaning, the number of BRDC cases and relapses was found to have progressively increased, the number of days until the first illness was found to have decreased (10.8 days vs. 22.5 days), and lower body weight and daily weight gain was observed compared to the group of calves previously not exposed to BRDC (Bach et al. 2011).

Overall, individual or small group housing is more favourable over large groups (Lorenz et al. 2011) and outdoor hutches (individual, pair or group) have better microclimatic conditions than shelters or calf barns, however, hutches require considerably more labour (Malá and Novák 2021). Although it is generally accepted that indoor housing poses greater challenges evading BRDC, analyzing studies published over the last 40 years could not clearly confirm it (Ollivett 2020). However, for successful calf rearing, good farm management and regular monitoring of calves can not be neglected even in case of small-group housing (Babu et al. 2009).

Microclimatic conditions

In terms of animal health and welfare, good quality of air is essential. It is determined by the design and operation of buildings and their ventilation systems, stocking density, body size, floor and litter material and its quality, and manure management (OIE 2021). It is not yet known exactly what air quality indicators can be associated with (sub) clinical pneumonia and other airway inflammations, but recent findings suggest that mean temperature, ammonia concentration, and air movement are the most important (van Leenen et al. 2020). For practical and economic reasons, measurements on the spot are usually performed on a single day (e.g. temperature and RH), but the concentration of air pollutants shows greater variability over time than in space (Groot Koerkamp et al. 1998). Most microclimatic indicators are characterized by diurnal variation and so their dynamics can be best examined with measurements lasting 24 h (Seedorf et al. 1998; van Leenen et al. 2020). Measurements should represent all phases of the farm work and take place at the height of the animals. In the first 8 weeks of life, dairy calves spend most of their time (about 70%) lying, so at this age, for example for NH_3 concentration, a height of 20–30 cm above the litter (Lago et al. 2006; Kaufman et al. 2015) and a height of 50 cm (van Leenen et al. 2021, 2020) are relevant. On the other hand, point and continuous measurements characterize the climatic indicators of the studied period, which may play a role in the maintenance of concomitant subclinical or clinical conditions, but the effect of climatic characteristics of the previous days, weeks or even longer periods can be assumed in their developement (van Leenen et al. 2020). Because of it, the use of digital data loggers for long-term registration of temperature and humidity can be valuable for monitoring ambient conditions (Müller 2021), especially if data are accessible in real time.

Temperature, relative humidity and wind speed

When designing housing conditions, we aim to create the most suitable microclimate for calves which is determined by the temperature of the air and surfaces inside the barn, humidity, wind speed, as well as the concentration of harmful gases, dust, and microbes (Roland et al. 2016). After birth, calves have functional thermoregulation, so as long as they are provided with the right amount of energy, dry bedding and a draft-free environment, they can adapt well to the outer temperature. Nonetheless, temperatures of 16–20 °C and 10–20 °C are recommended for bodyweights of up to 60 kg, and 60–150 kg, respectively, by a standard of the German Institute for Standardization (Roland et al. 2016). Low temperatures not alone but in combination with other adverse factors (humidity and wind) lead to increased morbidity and mortality: a Danish study shows that low temperatures and high RH (< 10 °C and > 85% RH) impair the health of calves (Nonnecke et al. 2009). The RH of livestock buildings depends on the ambient temperature, the amount of urine and faeces, the absorption capacity of the bedding and the effluent drinking water (Islam et al. 2019a). Warm air can hold more water, so with unchanged water content and increasing temperature, RH will decrease. There are few recommendations for humidity in naturally ventilated barns; according to Malá and Novák, optimal RH in calf barns and hutches should vary from 50 to 70–80% (Malá and Novák 2021; Müller 2021). Elevated RH may increase the effects of cold and draft, have a complex and indirect effect on survival and multiplication of respiratory pathogens (depending on their species and properties), increased Wisconsin scores (validated clinical scoring system for respiratory diseases) (McGuirk and Peek 2014) of calves when RH was elevated for 24 h, and increased basophil granulocyte counts were observed in bronchoalveolar lavage fluid (BALF) samples (van Leenen et al. 2020). A negative correlation has been observed between the minimum, maximum, and mean temperatures and RH, whereas a positive relationship has been found between the mean temperature of group pens and tissue lesions detected with ultrasound (van Leenen et al. 2020). On the other hand, low RH (< 50%) can dry the epithelial surface of the respiratory tract, leading to infections (Malá and Novák 2021).

Due to the optimization of humidity and the control of pathogens in the air, proper ventilation is essential, but draughty environment should be avoided (Table 1). Draughts with > 0.2 m/s velocity at low temperatures, and > 0.6 m/s at high temperatures shold be avoided (Malá and Novák 2021). Low (< 0.25 m/s) air speed is common in barns, which is unable to move the blades of wind wheel anemometers, in which case it is advisable to use a hot-wire anemometer (Fournel et al. 2017). Outdoor hutches are frequently installed on the leeward side of barns or placed in an open area where they are exposed to the wind (Malá and Novák 2021). The effect of air movement on respiratory diseases and thermal comfort of calves is often assessed in conjunction with ambient temperature, as air movement has a cooling effect, thus increasing cold stress. It can be mitigated by proper orientation (south or south-east) of the entrance of hutches during winter (Malá and Novák 2021). However, no correlation was found between air movement and temperature, and low temperature alone had no effect, so presumably the draught caused first airway inflammation and then developed further into pneumonia (van Leenen et al. 2020). Tissue lesions detectable by ultrasound may be present in a draughty environment (Buczinski et al. 2018a). In a study

Table 1. Recommended wind speed (m/s) in calf husbandry.

Recommendation	Circumstances	Above recommended values	References
≤ 0.25 m/s	Winter period		Webster 1984
≤ 0.2 m/s	At low temperature		Roland et al. 2016
≤ 0.6 m/s	At high temperature		Roland et al. 2016
< 0.5 m/s	Point measurement		Lundborg et al. 2005
< 0.8 m/s	Continuous (24-hour) measurements	OR for ≥ 3 cm lung lesions = 6.8 OR for ≥ 6 cm lung lesions = 15.9	van Leenen et al. 2020

OR = odds ratio

by van Leenen et al. (2020), the prevalence of lesions ≥ 1 cm was 81.8% in the draughty and 54.2% in the warm, dry, and ammonia-rich environment, compared to 31.6% under normal environmental conditions. However, ultrasonography cannot distinguish between acute and chronic processes, so no clear causal relationship can be drawn between lesions and momentary air movement.

Calf houses made of synthetic materials can create a favourable microclimate during cold, rainy, and windy conditions. In a winter study, although the average temperature in the calf hutch was only 2.5 °C higher than the outer temperature, wind speed was significantly lower and it was positively correlated with the occupancy rate of hutches (Hoshiba 1986). However, warm and humid conditions can be detrimental: an American study found that in summertime, it is on average 2 °C warmer in plastic calf hutches, and indoor RH is 8% higher than outer RH (Hill et al. 2011). High RH leads to condensation, i.e., moisture may condense on the walls of the calf hutch and the bedding and integument of calves may become wet (Roland et al. 2016). Climate change also makes it impact felt in Central Europe. During hot summers not only temperature and temperature-humidity index are critical, but also their duration is important in terms of heat stress (Kic 2022). Geographic direction has also some effect, as hutch entrance facing east or north could slightly mitigate the solar heat load in summer: although respiratory rates of calves and daily average temperatures did not differ between different compass points, morning and afternoon data differed relative to directions, moreover, calves in hutches facing east or north were seen more in shade than their fellows in south or west facing hutches (Bakony et al. 2021).

Harmful gases

Potentially harmful gases in barns are ammonia, carbon dioxide, carbon monoxide, dihydrogen sulphide, and methane (Roland et al. 2016). They are formed partly in physiological function of the animals or during decomposition of their excretions (faeces, urine), but they can result from certain technological processes. With continuous measurements, the daily dynamics of the concentration of each harmful gas can be plotted, and related technological processes can be identified (Zou et al. 2020). Concentrations of some barn gases are often around the lower detection limits of the devices, thus data obtained in this way should be treated with caution.

Ammonia

Ammonia (NH_3) is a colourless gas with a characteristic pungent odor that is evenly distributed in the air space of the barn (Rafai 2003). Of the barn gases, NH_3 may play the most important role in the development of respiratory diseases, as it directly damages the respiratory epithelium and decreases the number of ciliated epithelial cells (Brscic et al. 2010) which results in impaired mucociliary flow (Lundborg et al. 2005). NH_3 is water-soluble, thus forming corrosive ammonium hydroxide on the wet respiratory tract, damaging the epithelial barrier and paving the way for infection by pathogenic and opportunistic microbes (Brautbar 1998; Seedorf and Hartung 1999; Teye et al. 2008; van Leenen et al. 2020). At higher concentrations, tearing, nasal discharge, cough (Phillips et al. 2010) and corneal ulcers may also occur (Teye et al. 2008), but also indirectly play a role as a precursor to inorganic aerosol constituents (sulphates, nitrates, chlorides) in formation of the 2.5 µm particulate matter (PM2.5) fraction (Joo et al. 2015).

In cattle, excess nitrogen is converted to urea and excreted with urine, whereas undigested (feed, microbial, and endogenous) proteins are excreted with faeces, accounting for 70% and 30% of all selected nitrogen, respectively (Groot Koerkamp et al. 1998; Rafai 2003). Urea is converted to NH_3 by the microbial urease, and production and release of NH_3 depends on the temperature, RH, moisture and nitrogen content of the manure and on the husbandry technology; however, different NH_3 concentrations are not fully explained by temperature and RH (Seedorf and Hartung 1999). The detrimental effect depends not only on the concentration but also on the exposure time, the additional air pollutants and other environmental factors (Wathes et al. 2003).

There is no consensus on permissible NH_3 concentration (Table 2). The maximum acceptable values are 10–50 ppm depending on the species, exposure time, and country (Groot Koerkamp et al. 1998). Several studies have shown that in practice, NH_3 concentrations are lower than limits (Table 3) and open barns of dairy and beef farms have lower NH_3 concentrations than closed barns (Brscic et al. 2010). However, no clear relationship between the concentration and a detrimental effect has been described, so it is uncertain what NH_3 concentration is considered acceptable for dairy cows/calves (Seedorf and Hartung 1999; Kaufman et al. 2015). In calf prophylactories and closed calf barns, coughs and pneumonia are common at NH_3 concentrations above 30 ppm, whereas in closed barns, milk production is expected to decrease by 10% at NH_3 concentrations above 25 ppm (Rafai 2003). In pigs, exposure to 25 ppm NH_3 for 6 days resulted in elevated white blood cell counts in nasal lavage samples (Urbain et al. 1994), histological irritation of the nasal mucosa, and even functional impairment in tracheal smooth muscle contraction (Urbain et al. 1996). At relatively high (approx. 30–45 ppm) NH_3 concentrations, increased neutrophil granulocyte ratio and macrophage activity was detected in BALF samples from calves, suggesting active pneumonia, but these were no longer detectable 4 weeks after exposure (Phillips et al. 2010). In Switzerland, increased antibiotic use has been reported in beef calves with NH_3 concentrations ≥ 10 ppm (Schnyder et al. 2019). In pigs, however, the severity of nasal atrophy caused by *P. multocida* was significantly increased even at 5 ppm compared to 0 ppm NH_3 (Hamilton et al. 1996), i.e. the negative effect of NH_3 could be significant even at low concentrations. In calves, lung lesions of ≥ 1 cm were detected by ultrasound at NH_3 concentrations > 4 ppm. At an increasing NH_3 concentration, BALF samples showed elevated nucleated cell counts and increased epithelial cell ratios (van Leenen et al. 2020). Although in general, NH_3 concentrations below the guideline or limit values can be detected in calves' environment, its negative effect can be significant even at low concentrations, and other harmful gases and aerosols may be present in buildings that can increase airway damage as well. Chronic exposure to low NH_3 concentrations is also thought to play a role in the development of BRDC, thus exposure time and continuous measurements should be considered: e.g., in one study, NH_3 concentrations above 4 ppm were measured for an average of 0.51 ± 1.47 h per day (0–6.3 h) (van Leenen et al. 2020).

Gas tubes can be used for rapid NH_3 quantification. These should be corrected with barometric pressure according to the manufacturer's specifications, however, in farm conditions, acceptable values can be obtained without correction (Kaufman et al. 2015). Digital devices can detect several types of harmful gases in a barn (Lundborg et al. 2005), although some gases may cross-react due to the operation of the detectors (e.g. H_2S), resulting in false results.

Table 2. Recommended or permitted NH_3 concentrations (ppm) for livestock and human environment.

Recommendation	Species	Circumstances	References
≤ 25 ppm	Dairy cattle	Enclosed housing	OIE 2021
≤ 20 ppm	Animals and humans		CIGR 1984; EFSA 2009
≤ 10 ppm	Beef cattle	Insulated buildings	SCAHAW 2001
≤ 10 ppm	Not specified		Lundborg et al. 2005
≤ 10 ppm	Not specified	Mechanically ventillated calf barn	Woolums et al. 2009
50 ppm	Humans	PEL-TWA	OSHA 2021
25 ppm	Humans	REL-TWA	NIOSH 2021
35 ppm	Humans	REL-STEL	NIOSH 2021

PEL-TWA = Permissible exposure limit, time-weighted average
REL-TWA = Recommended exposure limit, time-weighted average
REL-STEL = Recommended exposure limit short-term exposure limits

Table 3. NH_3 concentrations in different cattle housing conditions.

Concentration	Animal type	Circumstances	References
0–8 ppm	Dairy cow	Litter / cubicle housing, Northern Europe (DE, DK, NL, GB	Groot Koerkamp et al. 1998)
0–8 ppm	Dairy calf	Litter or slat/group housing, Northern Europe (DE, DK, NL, GB)	
3.7 ppm	Calf	With and without litter, DE	Seedorf and Hartung 1999
6.4 ppm	Dairy cattle	With and without litter, DE	
4.7 ppm	Beef cattle	With and without litter, DE	
2.2 ppm (0–4 ppm)	Dairy calf	Pen air, winter, natural ventillation	Lago et al. 2006
1.4–3.0 ppm	Dairy cattle	Natural ventilation, free stall barn	Zhao et al. 2007
< 4 ppm (up to 15 ppm)	Veal calves	Indoors, fully slatted floor, ITA	Brscic et al. 2010
0.6–1.9 ppm	Dairy cow	Uninsulated loose housing, 10-min meauring points, EST	Kaasik and Maasikmets 2013
2.13 ppm (1.6 mg/m^3)	Dairy calf	Calf hutches and pens, single visit, CAN	Kaufman et al. 2015
< 1.87 ppm (< 1.4 mg/m^3)	Dairy calf	Barns with different housing types, weekly visit, CAN	
0.16–2.18, and 0.38–2.85 ppm	Dairy cow	Naturally ventilated barns, USA	Joo et al. 2015
1.7 ppm (up to 10 ppm)	Dairy and beef calves	Group housing (2-32 calves/group), BEL	van Leenen et al. 2020
0.66 ppm (0.07–2.00)	Dairy calves	Calf pens	Bonizzi et al. 2022

Some data suggest that there is no correlation between temperature and NH_3 or between RH and NH_3 concentration in cattle barns (Seedorf and Hartung 1999; Kaufman et al. 2015), whereas others claim that NH_3 concentration is temperature-dependent, showing a diurnal pattern, and is the highest in the afternoon (Teye et al. 2008). In a Chinese study, the increasing NH_3 concentration was explained by increasing temperature and increasing urease activity of manure during that time. However, low NH_3 concentrations were obtained at lower temperatures and higher RH, which may be due to the dissolution of NH_3 in water (Saha et al. 2014; Zou et al. 2020). In an other study, lower NH_3 concentrations were measured in March and May than in winter, whereas the ventilation rate (number of times the barn air was changed per hour) was higher in May and July compared to November (Joo et al. 2015). Keeping the bedding clean and dry helps to reduce NH_3

concentration, which can also be affected by bedding depth and ventilation (Kaufman et al. 2015). Others claim that there is no correlation between different air quality indicators (e.g., temperature, humidity, harmful gases) and bedding dryness (van Leenen et al. 2020). When the daily dynamics of NH_3 concentrations were analysed, elevated values were found when operating the manure removal device and at increased movement of the animals (feeding, milking), whereas at night, gradually decreasing concentrations were reported (Zou et al. 2020).

Hydrogen sulphide (H_2S)

H_2S is a colourless gas that is heavier than air, produced by the anaerobic bacterial breakdown of proteins and other sulphur-containing organic matter of manure. Its characteristic rotten egg odour can be smelled even at a < 300 ppb (< 0.3 ppm) concentration (Joo et al. 2015), although it only becomes truly unpleasant at around 3–5 ppm (OSHA 2019). According to the European Council, a maximum of 0.5 ppm is acceptable from an animal welfare point of view, but 5 ppm is permissible at manure removal, while its harmful effects may occur at ≤ 50 ppm and can lead to death at 350 ppm (CIGR 1984; EFSA 2009). Even at exposure to 50–100 ppm for one hour, it can cause mild conjunctivitis and anorexia in humans; at 200–300 ppm, severe cough may occur after one hour, and pulmonary oedema may occur with prolonged exposure. Exposure to lower concentrations can cause eye irritation, respiratory symptoms, and even loss of consciousness (Hooser et al. 2000). At high concentrations of 1 000–2 000 ppm, generalized seizures leading to respiratory paralysis and then death within 1–2 breaths, signs of histologically diffuse cerebral cortical laminar necrosis and oedema have been observed in cattle (Hooser et al. 2000; Joo et al. 2015). However, at concentrations of 100–150 ppm, humans lose their sense of smell (olfactory paralysis) and are therefore unable to assess the danger posed by the gas (OSHA 2019). If NH_3 concentration exceeds 25 ppm in calf housing, immediate action must be taken to reduce it (Malá and Novák 2021).

Limited data are available on the H_2S concentration in naturally ventilated stables (Table 4), which is presumably due to the fact that it is present at extremely low concentrations under normal conditions, with detectable concentrations increasing mainly during manure removal (CIGR 1984; Joo et al. 2015). Sudden deaths associated with the release of high concentrations of H_2S have been reported in cattle, pigs, and poultry, resulting also in loss of human lives (Hooser et al. 2000). A study in Washington, USA found no significant correlation between H_2S emission and ambient temperature and air movement (Joo et al. 2015). Regular removal of manure can reduce the accumulation of sulphur-containing compounds, thus preventing the formation of high H_2S concentrations.

Carbon dioxide

Carbon dioxide (CO_2) is a colourless and odourless gas that is heavier than air and is therefore concentrated in the air layer above the floor. It is mainly released into the air by being exhaled by animals; to a lesser extent, it is also formed during the decomposition of urine and faeces. Compared to atmospheric CO_2 concentration (0.038%, or 380 ppm),

Table 4. H_2S concentrations (ppb) in naturally ventillated cattle barns.

Concentration	Animal type	Circumstances	References
35–145 ppb	Dairy cow	Natural ventillation, Alberta, CAN	Clark and McQuitty 1987
2–32 ppb	Dairy cow	Natural ventillation, free stall barn, Ohio, USA	Zhao et al. 2007
7–14 ppb	Dairy cow	Natural ventillation, North Dakota, USA	Smith et al. 2006
0–59, and 0–136 ppb	Dairy cow	Natural ventillation, Washington, USA	Joo et al. 2015

indoor concentration can be up to 10 × higher, making it suitable for monitoring ventilation efficiency (Rafai 2003). The European Food Safety Authority (EFSA) has set a limit value of 3 000 ppm for CO_2 in livestock buildings (EFSA 2009), although experience has shown that 5 000 ppm CO_2 does not have a detectable adverse effect (Rafai 2003). Its concentration correlates strongly with the outside temperature and increases with the respiration of the animals (EFSA 2009). In pigs, a strong positive correlation between CO_2 and NH_3 concentrations was observed (Van Ransbeeck et al. 2013), while in cattle both gases showed the same trend (Zou et al. 2020). No such correlation was observed in calves, and correlations were found between individual health indicators and CO_2 only at higher concentrations than those measured in pigs (van Leenen et al. 2020). A positive relationship between RH and CO_2 was found in a Chinese dairy herd: as high RH is an indicator of poor ventilation, high CO_2 concentration can also be explained by this (Zou et al. 2020). If CO_2 pollution is not associated with other pollutants, it alone does not cause poisoning and reduced production. Its importance as an air quality indicator in calves is limited under practical conditions (Rafai 2003; van Leenen et al. 2020).

Other gases

Methane is a colourless and odourless gas lighter than air, mainly found in ruminants' barns. Its production is linked to rumen fermentation as it enters the atmosphere during regurgitation (Rafai 2003). It is important from the environmental point of view and has no limit value for animals or humans (EFSA 2009). Carbon monoxide is a colourless and odourless gas heavier than air and it accumulates directly above the floor (Rafai 2003). Its treshold is 10 ppm for animals (EFSA 2009). It is produced during imperfect combustion, mainly in case of faulty heating equipment in closed barns (e.g. poultry, pigs) or in use faulty engine vehicles (e.g. bedding), which in rare cases can cause problems in cattle barns.

Aerosols and aerial germ load

The totality of solid or liquid particles that also contain organic matter suspended in air for a long time is called bioaerosol. Depending on its size, each particle is able to remain in the air for a longer or shorter period of time, settling over time and being replaced by newly formed particles (Rafai 2003). Solid aerosol particles in livestock buildings are made up of organic matter of feed, litter, manure or animal origin (e.g. epithelial cells, hair, urine, faeces) and microorganisms, whereas liquid particles are condensed or released into the air during coughing and sneezing by animals or humans. Bioaerosols may contain other allergenic proteins, peptides, bacterial toxins, endotoxins, mycotoxins, but may also absorb barn gas molecules (Rafai 2003). Overall, bioaerosols can pose a particular risk to the health of animals and people in poorly ventilated buildings due to their high organic content (approximately 85–90%), higher concentration compared to other buildings, and their wide range of shapes and sizes (Rafai 2003; Tan and Zhang 2004; Cambra-López et al. 2010; Islam et al. 2020).

Particulate matter concentration

Solid and liquid particles suspended in (bio)aerosols can be defined as a complex mixture of particles with different physical (size, shape, density), chemical, and biological properties which determine the behaviour and effects of PM on the environment and health (U.S. EPA 2004; Cambra-López et al. 2010).

Of the air pollutants, PM particles can be the most reliably connected to human and animal diseases (Losacco and Perillo 2018), among others to respiratory diseases (Carpenter 1986). Particles are classified in a variety of ways according to their aerodynamic diameter (AED) in humans. The European Committee for Standardization divided the particles into 4 groups (so-called occupational health size fractions) according to their depth of passage in the human airways: (1) inhalable, (2) extrathoracic, i.e. does not get below the larynx, (3) thoracic (AED = 10 µm, get below the larynx), and (4) respirable (AED = 4 µm, reach the non-ciliated part of the airways) (Brown et al. 2013). The other classification divides particles into coarse (PM10) and fine (PM2.5) fractions according to the AED (European Comission 2008; EPA, 2020), but they also discribe an ultrafine (PM1.0) fraction (Losacco and Perillo 2018). The two classifications can be compared with penetration curves, the PM10 fraction is broadly similar to the thoracic (both 10–10 µm), while PM2.5 to the respirable fraction (2.5 and 4.0 µm, respectively). However, these classifications are based on adult humans. Because of the different anatomical and physiological characteristics of the respiratory systems of different animal species, other particle fractions may be connected to animal diseases (Ivester et al. 2014). These fractions stimulate the conjunctiva and respiratory tract. Although PM particles are removed by mucociliary clearance, the system can be overloaded at high PM concentrations, leading to influx of neutrophil granulocytes by phagocytic activity and cytokine production of macrophages (van Leenen et al. 2021). However, smaller particle fractions settle and accumulate in the lung parenchyma, inducing inflammation, impairing gas exchange, and thus indirectly burdening the cardiovascular system (Losacco and Perillo 2018).

The three main characteristics of PM in livestock buildings are: (1) it is present in a concentration of 10 to 100 times that of other indoor environments, (2) it binds odors and gases, and (3) it is biologically active, as it can contain many microorganisms (Cambra-López et al. 2010). Particluate matter particles are mostly larger, 2–10 µm in size (Cambra-López et al. 2010), while others report that fine (0.3–2.0 µm) fractions occurred at higher concentrations than coarse (2.0–10 µm) fractions (Islam et al. 2019a,b). Due to their higher mass, particles with a size of 5–10 µm remain suspended in air for a short time and settle quickly (Islam et al. 2019a).

PM concentration is significantly influenced by the species, husbandry, feeding technology, stocking density and animal activity, ventilation type and efficiency, as well as the season and time of day. For example, poultry farming has a higher concentration of PM compared to pigs, and pig barns are also dustier than cattle barns. Furthermore, as the stocking density increases, so does PM concentration, or higher concentrations can be measured during the day than at night, according to the animals' activity (Tan and Zhang 2004). In the context of calf rearing, it would be important to identify specific substances and activities as sources of PM and take measures to reduce them, as even very small (ultra-fine, PM1.0) dust particles can play a significant role in the development of calf pneumonia (van Leenen et al. 2021).

The effect of each fraction depends on both the concentration and the exposure time. For humans, the 24-hour average PM concentration recommended by WHO is up to 25 µg/m^3 and 50 µg/m^3 for PM2.5 and PM10 fractions, respectively, while on annual basis 10 µg/m^3 and 20 µg/m^3, respectively, are accetable (WHO 2005). There is no recommendation for animals in relation to BRDC, and relatively little information is available on the PM characteristics of calf barns in Europe, mainly based on point measurements or up to a few days of continuous measurement (van Leenen et al. 2021). Concentrations of PM2.5 and PM10 fractions were similar to WHO limits in several studies (Table 5), however, up to 5–30 × higher one-hour averages were also reported (van Leenen et al. 2021).

The relationship between temperature and RH as well as aerosol formation has been described in scientific literature. Some authors report higher concentrations of aerosols in winter (Tan and Zhang 2004), while others have found lower concentrations of aerosols in winter compared to spring (Islam et al. 2020). Other results suggest that PM emission is positively correlated with ambient temperature and negatively correlated with RH (Joo et al. 2013). In calf barns, concentration of fine aerosol particles (0.5–5.0 µm but mainly 1.0–2.0 µm) increases in the summer–autumn period, and so there is a positive correlation

Table 5. Particulate matter (PM) concentrations (μg/m^3) in naturally ventilated cow barns.

Fraction	Concentration (μg/m^3)	Circumstances	Reference
PM1.0	7.7–12.6	Dairy cow, uninsulated loose housing, 10-min meauring points	Kaasik and Maasikmets 2013
PM1.0	16.0 (0.28–43.9)	Dairy housing, 24-h measurments	van Leenen et al. 2021
PM1.0	17.5 (0.20–77.1)	Beef housing, 24-h measurments	van Leenen et al. 2021
PM2.5	13.6–23.6	Dairy cow, uninsulated loose housing, 10-min meauring points	Kaasik and Maasikmets 2013
PM2.5	22.3 (0.49–50.30)	Dairy housing, 24-h measurments	van Leenen et al. 2021
PM2.5	29.1 (0.60–144.90)	Beef housing, 24-h measurments	van Leenen et al. 2021
PM10	38.3–119.5	Dairy cow, uninsulated loose housing, 10-min meauring points	Kaasik and Maasikmets 2013
PM10	58.1 (1.60–141.10)	Dairy housing, 24-h measurments	van Leenen et al. 2021
PM10	86.3 (4.60–251.20)	Beef housing, 24-h measurments	van Leenen et al. 2021

with indoor and outdoor temperature (Islam et al. 2019a). It may be explained by the fact that high temperature, low RH, and air movement (especially in drafty conditions) contribute to the drying and dusting of bedding, and dust is released into the air due to increased animal activity and air movement (Joo et al. 2013; Islam et al. 2019a; Urso et al. 2021). Nevertheless, no correlation was found between the concentration of 5–10 μm fractions and the temperature (Islam et al. 2019a). At > 70% RH, the concentration of aerosol particles is low, presumably due to the aggregation of the particles (Takai et al. 1998; Cambra-López et al. 2010) by which the larger (5–10 μm) particle fraction settles quickly and remains suspended in air for a short time. In contrast, the concentrations of smaller aerosol fractions (0.5–5.0 μm) have been shown to be positively correlated with RH (Islam et al. 2020). However, in 24-hour measurements in Belgian herds (24 dairy and 23 beef), no relationship was found between PM concentrations and a number of environmental variables such as temperature, RH, air movement, aerial germ load, NH_3 and CO_2 (van Leenen et al. 2021). Others also report no correlation between PM concentration and the stocking density in calf stables (Islam et al. 2020).

Any activity at the farm, sunrise and sunset, and other factors that increase the agitation and activation of the animals (e.g. light periods in poultry, feeding in pigs) may lead to an increase in the formation of PM particles that may become airborne (Cambra-López et al. 2010). A diurnal PM profile was observed in naturally ventilated dairy barns: PM2.5 and PM10 concentrations also peaked late in the evening, while they were lowest from night to morning. There was a strong positive correlation between hourly PM2.5 and PM10 concentrations and temperature (R = 0.8 and 0.9), but increased activity of animals had no significant effect, albeit lower morning peaks were observed in relation to feeding (Joo et al. 2013). In a continuous sampling survey, four types of PM concentration patterns were identified in all three PM fractions: (1) no peak values, (2) more minor, (3) more major, (4) more minor and one major peak, during the day. Of these, pattern 3 was the most common, occurring in 51% of the herds. Peak values are thought to be related to bedding or feeding, as they are the most important sources of PM, but can also be influenced by ventilation and animal movement (van Leenen et al. 2021). Humidifiers can be used to reduce PM concentration as aerosol particles aggregate and settle at higher RHs. In humid environments, however, airborn microorganisms can survive, while the efficiency of evaporative heat loss deteriorates during heat stress. However, the use of equipment for an appropriate period of time (before dusting events, increased animal activity) may be beneficial (Amosson et al. 2006). In addition, as the activity of cattle increases in the evening, dust formation can also be reduced by timing the feeding so that rumination is shifted during the period of increased activity (Urso et al. 2021).

Aerial germ load

Bioaerosols on farms can serve as vectors for microorganisms (bacteria, fungi) or even endotoxins (Islam et al. 2019a). Bacteria in the air come mainly from the animal's body surface, manure, and bedding, but can also be released into the air by exhalation and coughing in respiratory disease (Webster 1984), meaning that the main source of bacteria is the calf itself (Hill et al. 2011). Previous research provides no clarity on the relationship between high bacterial counts and respiratory disease. Although most of the bacteria in the air are non-pathogenic, even dead airborn bacteria burden the respiratory defense mechanisms (Wathes et al. 1983). It has long been hypothesized about (Webster 1984) and studies with filtered air (lower germ count and dust) have shown a link between the aerial germ load and respiratory disease (Pritchard et al. 1981; Hillman et al. 1992). The association of some environmental factors with respiratory diseases has been studied in naturally ventilated barns; the prevalence of respiratory diseases increased with increasing aerial germ load in individual calf cages (Lago et al. 2006). However, previously no difference was found in the incidence of respiratory diseases at barns with significantly different numbers of airborn bacteria and fungi (Blom et al. 1984). In a Japanese dairy herd, a positive correlation was found between the aerosol fraction of 0.3 to 5.0 μm and the concentration of aerobic bacteria in the air (Islam et al. 2020). According to a study in a laying flock, the vector role is mainly characteristic of particles > 3.3 μm (Zheng et al. 2013). As these particles can already reach the deeper airways, their role in the disease cannot be ruled out.

Determination of the aerial germ load is not aimed at isolating and counting specific bacteria, but the total number of germs (CFU/m^3) obtained can be considered as an air hygiene marker (Nordlund 2008). The plates typically show a mixed bacterial flora, usually consisting of *Staphylococcus*, *Streptococcus*, *Bacillus* sp. and *Escherichia coli*. Sampling and evaluation are hampered by the fact that a number of tools (e.g., impaction systems) have been developed to monitor clean rooms, however bacteria outgrow the plate even under very small volume of air samples in barn conditions (Nordlund 2008). The number of germs in the outdoor air is usually from 100–1 000 CFU/m^3 up to 20 000 CFU/m^3. A typical aerial germ load inside an individual calf hutch is 20 000 CFU/m^3 but it can reach 100 000 CFU/m^3 when the bedding is stirred by the calf. In contrast, aerial germ loads of 5 000 to 30 000 CFU/m^3 are possible in well-ventilated barns; while with poor ventilation, up to 100 000 CFU/m^3 or even millions of CFU/m^3 may be present, in which case respiratory symptoms (enzootic pneumonia) are common (Nordlund 2008). Of course, thousands of colonies on agar plate are difficult or even impossible to count, but a dilution series can be used to make a good estimation for 1 m^3 of air (Islam et al. 2019a). Studies in calf barns have shown large differences in the aerial germ load depending on the season and location (Table 6).

The clearance of microorganisms entering the air is primarily determined by dehydration and ventilation; to a lesser extent, by sedimentation and inhalation by animals (Webster 1984). Most bacteria are sensitive to dehydration, dying in seconds within becoming airborn, however, with an RH above 75–80%, they can generally survive for minutes (depending on the species) and then bacterial density of the air increases significantly (Webster 1984; Nordlund 2008; Malá and Novák 2021). The RH of cold air is high even with the same absolute amount of water, which explains the higher incidence of respiratory and diarrhoeal diseases in winter (Gulliksen et al. 2009a); whereas in summer, warmer air and lower RH contribute to the dehydration of bacteria and lower aerial germ load. No association was found between different airborn bacteria and RH in a Japanese study, presumably

Table 6. Airborne bacterial counts in calves' environment (CFU/m^3).

	CFU/m^3			
Value	Absolute	log$_{10}$	Circumstances	Reference
Average	112 280	4.05	Pens in naturally ventillated calf barns, winter	Lago et al. 2006
Min	29 644	4.47		
Max	> 326 418	> 5.51		
Average	44 482	4.65	Alley in naturally ventillated calf barns, winter	Lago et al. 2006
Min	5 274	3.72		
Max	> 326 418	> 5.51		
Average	14 125	4.15	June-October	Islam et al. 2019a
Max	52 481	4.72	September	
Average	1 479	3.17	November - May 4-5 month old calves	Islam et al. 2020
Min	417	2.62	February	
Max	4 571	3.66	March	
Average	247 002	5.39	Dairy and beef calves, straw bedding, January-April	van Leenen et al. 2020
Min	28 000	4.45		
Max	400 000	5.60		
Average	32 359	4.51	Dairy calf pens, winter season	Bonizzi et al. 2022
Min	2 344	3.37		
Max	131 825	5.12		

CFU - colony forming units

due to significant differences in RH during their investigations (Islam et al. 2019b). The effect of temperature on airborn microorganisms has not been fully elucidated (Zhai et al. 2018) but some authors suggest a strong positive correlation between the temperature and aerial germ load (Islam et al. 2020). No correlation was found between the total bacterial count and aerosol concentration, either (Islam et al. 2019a). The number of germs in the air also depends on stocking density, e.g. when it doubles, a tenfold ventilation cannot fully compensate for the aerial germ load (Webster 1984). Studies by Lago et al. (2006) and van Leenen et al. (2020) obtained different mean bacterial counts (112 280 vs 247 000 CFU/m^3) in calf environment, which may be explained by different ages resulting in different body surfaces as the source of germs, or individual vs group housing. Others, however, did not find a significant correlation between individual aerosol fractions and stocking density, or between airborne aerobic bacterial concentration and stocking density (Islam et al. 2020).

Gram-negative bacteria are ubiquitous in animal buildings and are present in relatively large numbers in the air of calf barns, therefore the role of endotoxins in airway inflammations should also be considered (Islam et al. 2019a). Which part of the airways it reaches depends on the size of aerosol particles (van Leenen et al. 2021); chronic respiratory diseases attributable to PM and endotoxin inhalation have been reported in horses (Ivester et al. 2014). Neutrophil granulocytes release tissue-damaging enzymes under the influence of endotoxins but in the case of tolerance, the cell response may fail. Moreover, even the response of macrophages to subsequent microbial stimuli may be reduced, decreasing the inflow of neutrophils, and thus susceptibility to disease may be increased (Miyata and van Eeden 2011; Sahlander et al. 2012; van Leenen et al. 2021). It is assumed that just as has been described for farmers, tolerance develops in calves due to major endotoxin loading from birth. This is indicated by the fact that no neutrophil inflammatory response was found when analysing a BALF sample. Furthermore, a slightly higher endotoxin concentration than that causing tolerance but not yet causing an acute respiratory problem can lead to chronic inflammation, resulting in a steadily elevated basal neutrophil concentration that rises only at significant peak PM values (van Leenen et al. 2021). No correlation was found between PM and endotoxin concentrations in calf barns, however, an endotoxin activity reported in endotoxin units (EU) was 8.5 EU/µg in the PM10 fraction was observed for the incidence of lung tissue lesions of ≥ 1 cm, which occurred in 11.4% of the study herds (van Leenen et al. 2021).

Conclusion

Due to the multifactorial nature of BRDC and the different production systems, reduction of pathogen exposure, strengthening resistance and immunity, and improvement of husbandry conditions can be considered as preventive strategies (Stokstad et al. 2020). With increased environmental control, the effects of the climatic factors on calves' health can be more easily identified and measures can be taken to reduce them, preventing the occurrence of and damage done by possible diseases, mainly respiratory ones such as BRDC.

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