Veterinary Pathology
2023, Vol. 60(2) 226–234

Article reuse guidelines:
sagepub.com/journals-permissions
DOI: 10.1177/03009858221146096
journals.sagepub.com/home/vet

Bronchopneumonia with interstitial pneumonia in feedlot cattle: Epidemiologic characteristics of affected animals

Luke A. J. Haydock[1], R. Kent Fenton[2], Dani Smerek[2], David L. Renaud[1], and Jeff L. Caswell[1]

Abstract

Bronchopneumonia with interstitial pneumonia (BIP) of feedlot cattle is characterized by gross and histologic lesions of cranioventral bronchopneumonia (BP) and caudodorsal interstitial pneumonia. This study described the characteristics and frequency of BIP in western Canadian feedlot cattle and identified epidemiologic differences between BIP and either BP or acute interstitial pneumonia (AIP). The study of 9909 deaths on 4 western Canadian feedlots included 1105 BIP, 1729 BP, and 878 AIP cases. A population of 55 cases with gross, histopathology, and microbiology data was used to validate the primary data set. BIP was the second most common reason for death (or euthanasia) from respiratory disease (1105/9909 cases), and the observed frequency was twice what was expected from random concurrence of BP and AIP. Based on logistic regression models, epidemiologic characteristics of BIP were comparable to those of BP, although BIP cases were more chronic with more instances of clinical illness prior to death. BIP was epidemiologically distinct from AIP. Specifically, BIP more frequently affected steers than heifers, deaths occurred earlier in the feeding period at lower body weights and lower daily weight gains, and BIP cases had longer durations from the first clinical illness to death and more separate instances of clinical illness prior to death. Furthermore, death from BIP mainly occurred in winter and fall, while death from AIP was most frequent in summer. These findings define BIP as a unique condition of feedlot cattle and suggest that chronic BP may promote the development of fatal interstitial lung disease in at-risk cattle.

Keywords

atypical interstitial pneumonia, beef, bovine respiratory disease, calves, epidemiology, lung, pathology, pathogenesis

Bronchopneumonia with interstitial pneumonia (BIP) of feedlot cattle is a postmortem diagnosis involving lesions of bronchopneumonia in the cranioventral lung regions and lesions of interstitial pneumonia (IP) in the caudodorsal lung regions.[4] Acute interstitial pneumonia (AIP; also known as atypical interstitial pneumonia) is a widely recognized and economically significant disease in feedlot cattle[3,13] that typically is acutely progressive with a high case fatality rate, and predominantly occurs in well-conditioned heifers late in the feeding period.[14] Research and review papers on AIP in feedlot cattle mention a high frequency of concurrent BP in affected animals. This has been termed feedlot IP (ie, a "variant" of feedlot AIP) or secondary IP,[2,9] but BIP is the favored term based on the morphologic features used for diagnosis.[4]

We compared pathologic and microbiologic findings in fatal cases of BIP, BP, and AIP in beef feedlot cattle.[4] In BIP cases, the cranioventral lesions of BP were usually chronic, whereas the caudodorsal lesions of alveolar and bronchiolar damage were usually acute, implying that the cranioventral BP preceded the interstitial lung disease. This, along with the finding that *Mannheimia haemolytica* genotype 2 was less frequently isolated from the cranioventral lung of BIP compared with BP cases, implies that the cranioventral lung of BIP cases was more often affected by a more chronic disease involving less-virulent or secondary bacteria compared with that of BP. The results suggested that in BIP cases, chronic inflammation resulting from bacterial infection of cranioventral lung might increase the sensitivity to a lung toxicant (eg, 3-methylindole), with subsequent damage to alveoli and bronchioles.[4]

It is not known if BIP is a unique disease process or a chance concurrence of BP and AIP.[2,5,11,14] Anecdotal reports suggest that BIP is a common diagnosis in feedlot cattle, yet there is a

[1]University of Guelph, Guelph, ON, Canada
[2]Feedlot Health Management Services, Okotoks, AB, Canada

Supplemental Material for this article is available online.

Corresponding Author:
Jeff L. Caswell, Department of Pathobiology, Ontario Veterinary College, University of Guelph, Guelph, ON N1G 2W1, Canada.
Email: jcaswell@uoguelph.ca

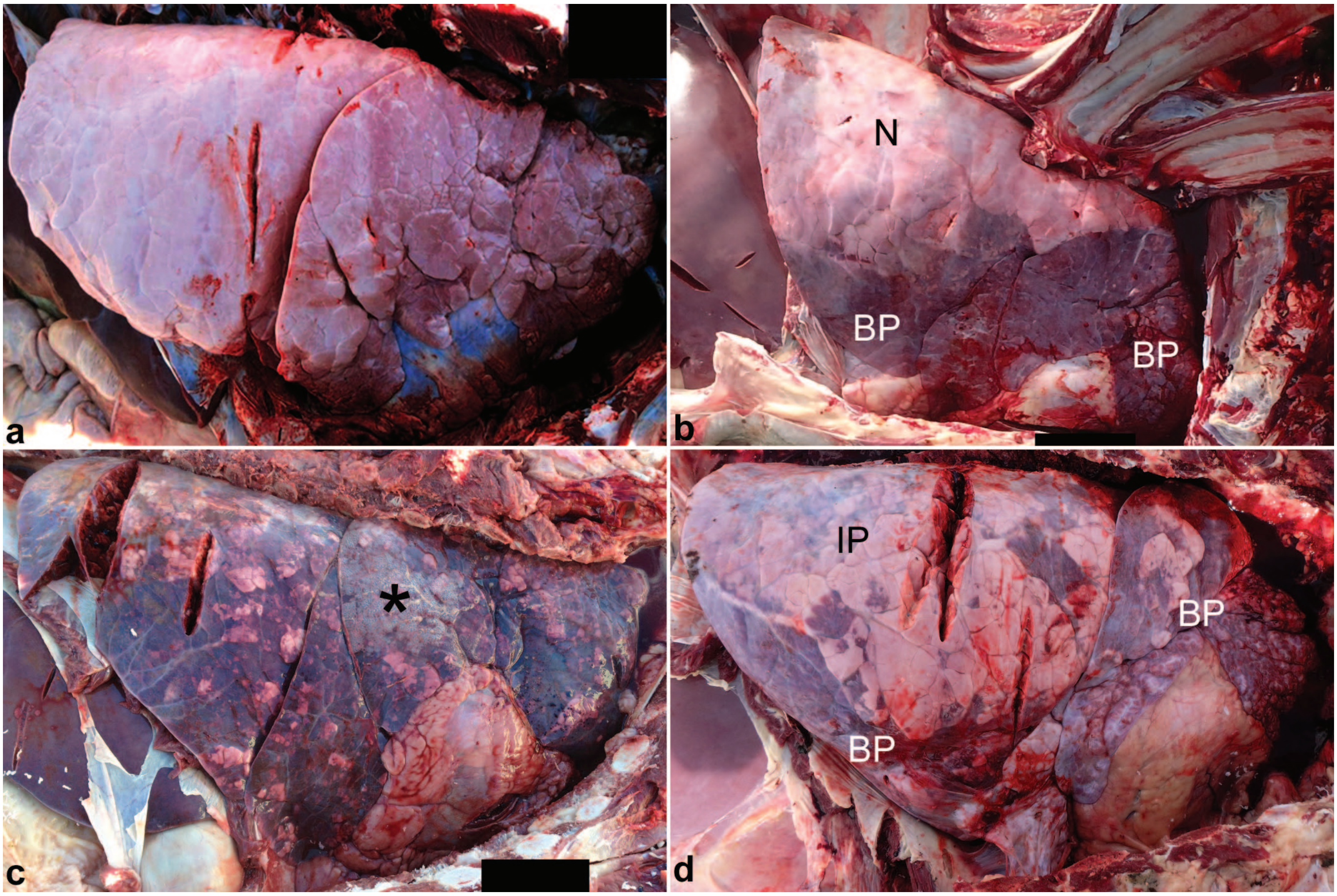

Figure 1. Gross lung lesions in cases of bronchopneumonia (BP), acute interstitial pneumonia (AIP), and bronchopneumonia with interstitial pneumonia (BIP) in feedlot cattle. (a) Normal lung. (b) BP. The cranioventral lung (BP) is red-purple and sharply demarcated from the normal caudodorsal lung (N). (c) AIP. Throughout the lung, most tissue is purple, whereas some lobules have a normal pink color. The lung fails to collapse and appears overinflated, with slight bulging from the cut surface, and subpleural and interlobular emphysema is present (*, and cut surface). (d) BIP. The caudodorsal area (IP) has lesions similar to AIP described above. The cranioventral area (BP) is red-purple as described above for BP.

considerable deficit in knowledge of the nature of the interaction between BP and IP. The aim of this study was to describe the frequency and epidemiologic characteristics of western Canadian feedlot cattle with pathologic diagnoses of BIP and to identify epidemiologic differences between BIP and either BP or AIP.

Materials and Methods

Primary Data Set

This study evaluated mortalities (natural death or euthanasia) on 4 western Canadian commercial beef feedlots between January 2016 and January 2020. Feedlots were included in the study on the basis of (1) having a high frequency of BIP cases and (2) a protocol for performing a standardized postmortem examination of all deaths with postmortem photos taken and reviewed by feedlot veterinarians. Animal health and management data were collected and made available by Feedlot Health Management Services (Okotoks, Alberta).

The primary data set included 9909 cases with postmortem diagnoses made by feedlot veterinarians following a review of gross postmortem lesions (in-person or based on a standardized set of photographs) as part of the routine delivery of services by Feedlot Health Management Services to commercial beef feedlots. In general, BP was characterized by purple to dark-red lesions in the cranioventral lung regions that were sharply demarcated from the unaffected caudodorsal lung (Fig. 1a). Some BP cases had 1 or more of the following variants within the cranioventral lesions: homogeneous consolidated lung, fibrin within lung tissue or on the pleural surface, abscesses, or caseous foci. Lung lesions of AIP had a generalized distribution, often an alternating pattern of pale pink to dark-purple lobules ("checkerboard pattern"), with overinflation or failure to collapse, bulging of lung tissue on cut surface, and interlobular edema and/or emphysema (Fig. 1b). BIP cases had both lesion types: BP in the cranioventral region and AIP in the caudodorsal region (Fig. 1c). Cases were assigned to 1 of the 5 diagnosis groups: BIP, AIP, BP, "other" bovine respiratory disease (O-BRD), and non-BRD. The BP group included cases with fibrinous pneumonia, bronchopneumonia, chronic pneumonia, caseonecrotic bronchopneumonia, and bronchopneumonia with arthritis. The O-BRD group included cases with chronic pleuritis, lung abscess, infectious bovine rhinotracheitis, or cases of pneumonia that did not fit the above categories. The non-BRD group included cases with gastrointestinal disease, musculoskeletal disease, injuries, and other nonrespiratory diagnoses. Data for 18 cases with a gross diagnosis of viral pneumonia were excluded from comparisons of BIP, BP, and AIP because they were infrequent and not easily assigned to these diagnosis groups. The 9909 cases in the study population included 1105 BIP, 1729 BP, 878 AIP, 133 O-BRD, 6046 non-BRD cases, and the 18 cases of viral pneumonia that were excluded from the comparison of BIP, BP, and AIP.

Some cases had incomplete data. Of the 9909 cases, 69 (0.7%; including 4 BIP, 10 BP, 3 AIP, and 52 non-BRD) were missing arrival weights and were omitted from analysis of arrival weight and average daily weight gain. Average daily weight gain was estimated by subtracting arrival weight from postmortem weight and dividing by the number of days on feed; 127 cases with gains calculated to be greater than 4.5 kg/day or less than-4.5 kg/day were arbitrarily presumed to be errors and were omitted from the analysis.

Descriptive statistics were compared among postmortem diagnosis groups, including the proportion of deaths attributed to BIP, sex distribution (steers, heifers, or bulls), postmortem weight, days on feed, average daily weight gain, days from the first signs of clinical illness until death, number of separate instances of clinical illness prior to death, season of death, and presence of fever upon arrival to the feedlot.[4] For this study, clinical illness was restricted to temporally separated incidents diagnosed as "arrival fever," "undifferentiated fever," "no fever," or "AIP."

Validation Data Set

A smaller data set of 55 cases with more extensive postmortem investigation was included to validate the findings in the primary data set of 9909 cases. These 55 cases were sampled from 6 beef feedlots in Alberta and Saskatchewan, Canada, from January 2018 to January 2022, and included 18 BIP, 24 BP, and 13 AIP cases. The gross and histopathology, microbiology, and other findings are reported elsewhere.[4] Of these 55 cases, 25 were included in the primary data set of 9909 cases. In contrast to the primary data set, in which assignment of cases to study groups was based on gross diagnoses made by multiple feedlot veterinarians, diagnoses in these 55 cases were based on histological diagnosis (Fig. 2) following gross diagnosis by a single feedlot veterinarian (RKF, who also made some diagnoses in the primary data set). Cases of O-BRD and non-BRD were not included in the data set of 55 cases.

Statistical Analysis

Categorical variables were compared using chi-square tests. For continuous variables, data were first tested for normality and equality of variance using the Shapiro-Wilk test and Levene's test, respectively. When data for the continuous variables were not normally distributed, significant differences between diagnosis groups were determined by the Mann-Whitney *U*-test, and median values and interquartile ranges (IQRs) were reported. Otherwise, for normally distributed data with equal variances between groups, significant differences were determined by Student's *t*-test, and mean values and 95% confidence intervals were stated. $P < .05$ was considered significant. In addition, a logistic regression model was constructed to analyze the variables that had the greatest impact on the probability of BIP mortality compared with all other causes of death. Statistical analyses were performed with R software packages implemented via an open-source statistics interface (JASP, University of Amsterdam).

Results

Descriptive Analysis, Primary Data Set

Of the 9909 cases in the primary study, 6214 (62.7%) were steers, 3609 (36.4%) were heifers, and 86 (0.9%) were bulls. Upon arrival to the feedlot, the median body weight was 267 kg (IQR = 230–315 kg). The median body weight at death was 386 kg (IQR = 283–526 kg). Only 76 (0.8%) of these animals had a record of fever upon arrival to the feedlot. Cattle spent a median of 112 days (IQR = 51–198 days) at the feedlot prior to death. The average time from onset of clinical signs to death was 27 days (median = 0 days; IQR = 0–26 days). The number of instances of clinical illness prior to death were none (5129 cases, 51.8%), 1 (2364 cases, 23.9%), 2 (1151 cases, 11.6%), 3 (602 cases, 6.1%), or ≥4 (663 cases, 6.6%). Most deaths occurred in winter (3647 cases, 36.9%), with fewer in spring (2388, 24.1%), fall (1964, 19.9%), or summer (1892, 19.1%).

Diagnoses in the 9909 cases included BIP (1105 cases, 11.2%), different forms of BP (1729 cases, 17.4%), AIP (878 cases, 8.9%), viral pneumonia (18 cases, 0.2%), O-BRD (133 cases, 1.3%), and non-BRD (6046 cases, 61%). Thus, BIP was the second most frequent reason for death (or euthanasia) from respiratory disease. To investigate the possibility that BIP is simply a chance concurrence of BP and AIP, the expected frequency of concurrence was calculated as ([BP + BIP]/total) × ([AIP + BIP]/total) × 100%. Based on these data, the expected frequency of animals having both lesions (BP and AIP) was 567 cases (5.7%), whereas the observed frequency of BIP was 1105 cases (11.2%); that is, 1.96-fold higher than what was expected with chance concurrence of BP and AIP ($P < .001$, chi-square test).

Of the 1105 BIP cases (Table 1), most were steers ($n = 739$, 66.9%), with fewer heifers ($n = 360$, 32.6%) and bulls ($n = 6$, 0.5%). Upon arrival to the feedlot, the median weight of animals eventually dying of BIP was 254 kg (IQR = 215–293 kg), and their median weight at death was 318 kg (IQR = 254–395 kg). BIP cases spent a median of 101 days (IQR = 56–153 days) at the feedlot prior to death and had a median daily gain of 0.61 kg/day (IQR = 0.13–0.98 kg/day) from arrival to death.

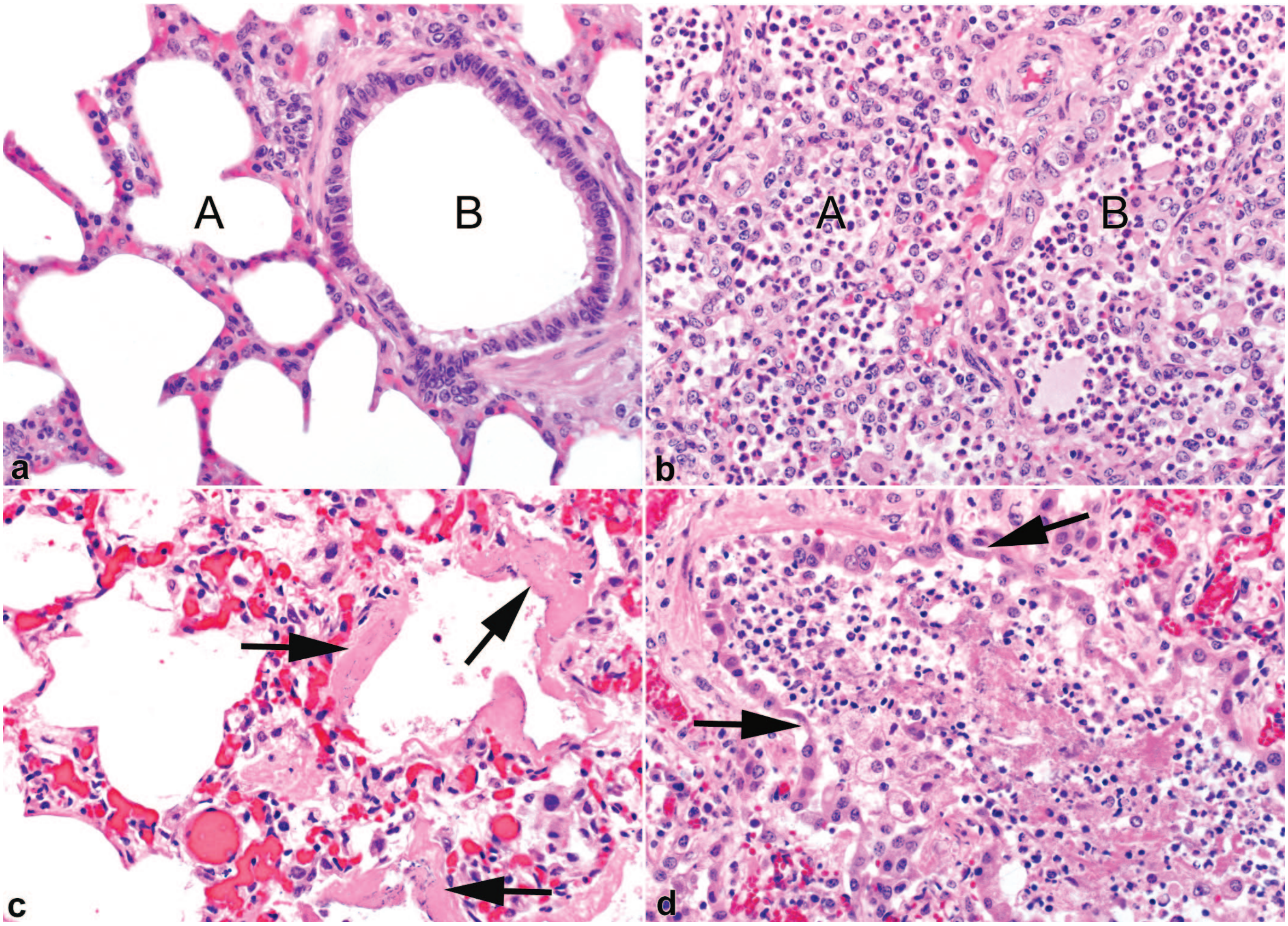

Figure 2. Histologic lung lesions in feedlot cattle. (a) Normal lung including alveoli (A) and bronchiole (B). (b) The alveoli (A) and bronchiole (B) are filled with neutrophils and macrophages, as would be present in cases of either bronchopneumonia (BP) or bronchopneumonia with interstitial pneumonia (BIP). Attenuation of bronchiolar epithelium is present but is not required for the diagnosis of BP. (c) Alveoli are lined by eosinophilic hyaline membranes (arrows). (d) The bronchiolar epithelium is attenuated (arrows). Neutrophils and macrophages are present in the lumen but are not required for the diagnosis of acute interstitial pneumonia (AIP) or BIP. Alveolar hyaline membranes (c) or type II pneumocyte proliferation are required for the diagnosis of AIP or BIP and bronchiolar necrosis (d) is typically present in these cases.

Only 7 cases (0.6%) were febrile upon arrival to the feedlot. The median time from onset of clinical signs to death from BIP was 19 days (IQR = 1–71 days). Of 1105 BIP cases, 256 (23.2%) had no clinical illness prior to death, 298 (27.0%) had 1 instance of clinical illness, 212 (19.2%) had 2 separate instances, 159 (14.4%) had 3 instances, and 180 (16.3%) had ≥4 instances. The majority of BIP cases occurred in winter (533, 48.2%), with fewer in spring (283, 25.6%), fall (156, 14.1%), and summer (133, 12.0%).

Comparison of Diagnosis Groups, Primary Data Set

Comparing BIP with BP cases, BIP cases included a significantly lower proportion of steers (66.9% vs 72.1%) and bulls (0.5% vs 1.3%), and a higher proportion of heifers (32.6% vs 26.6%; $P < .001$; Fig. 3a, Table 1). Median body weights on arrival to the feedlot were only marginally lower for cases eventually dying of BIP versus BP (254 kg vs 261 kg; $P = .004$), whereas median body weights at death were significantly higher in BIP cases (318 kg vs 277 kg; $P < .001$; Fig. 3b), and BIP cases were in the feedlot longer before death than BP cases (101 days vs 61 days; $P < .001$; Fig. 3c). BIP cases had a higher median daily gain from arrival to death than BP cases (0.61 kg/day vs 0.24 kg/day; $P < .001$). The time from the first clinical illness to death was longer for BIP versus BP cases (19 days vs 15 days; $P < .001$, Fig. 3d) and more BIP cases had ≥2 separate instances of clinical illness prior to death (49.9% vs 44.7%; $P = .008$; Fig. 3e). BIP cases (compared with BP cases) were less common in winter (48.2% vs 54.2%) and fall (14.1% vs 17.1%), and more common in spring (25.6% vs 20.8%) and summer (12.0% vs 7.9%; $P < .001$ across all 4 seasons; Fig. 3f).

Comparing BIP with AIP cases, BIP cases included a lower proportion of heifers (32.6% vs 62.5%) and a higher proportion of steers (66.9% vs 37.4%) and bulls (0.5% vs 0.1%; $P < .001$; Fig. 3a; Table 1). Median body weights on arrival to the feedlot were similar for BIP versus AIP cases (254 kg vs 254 kg; $P =$

Table 1. Epidemiological characteristics of 9909 deaths on 4 western Canadian feedlots between January 2016 and January 2020.

	BIP (n = 1105)	BP (n = 1729)	AIP (n = 878)	O-BRD (n = 133)	Non-BRD (n = 6046)	OR	P Value
Sex (%)							
Steer	66.9	72.1	37.4	66.9	62.9	1.23	0.002
Heifer	32.6	26.5	62.5	32.3	36.2	0.8	0.001
Bull	0.5	1.3	0.1	0.8	0.9	0.6	0.22
Arrival weight (kg; median, IQR)	254 (214–293)	261 (223–298)	254 (218–294)	262 (229–300)	274 (235–332)	n/a	<0.001
Fever at arrival (%)							
Yes	0.6	1.2	0.8	0.0	0.7	0.8	0.59
No	99.4	98.8	99.2	100.0	99.3	1.25	0.59
No. illnesses (%)							
0	23.2	28.2	34.3	57.1	66.2	0.24	<0.001
1	27.0	27.1	38.4	18.8	20.3	1.2	0.01
2	19.2	16.2	19.0	10.5	7.9	1.99	<0.001
3	14.4	12.1	5.6	6.8	2.9	3.17	<0.001
≥4	16.3	16.4	2.7	6.8	2.7	3.35	<0.001
First illness to death (days; median, IQR)	19 (1–71)	15 (0–48)	1 (0–12.3)	0 (0–50)	0 (0–7)	n/a	<0.001
Arrival to death (days; median, IQR)	101 (56–153)	61 (32–108)	180 (119–239)	156 (85–226)	127 (52–215)	n/a	<0.001
Postmortem weight (kg; median, IQR)	318 (254–396)	277 (227–352)	465 (390–545)	431 (329–568)	443.5 (318–563)	n/a	<0.001
Average daily gain (kg/day; median, IQR)	0.61 (0.13 to 0.98)	0.24 (−0.39 to 0.8)	1.12 (0.92 to 1.35)	0.98 (0.5 to 1.43)	1.01 (0.45 to 1.38)	n/a	<0.001
Season of mortality (%)							
Fall	14.1	17.1	13.4	15.8	22.7	0.63	<0.001
Winter	48.2	54.2	24.0	32.3	31.8	1.69	<0.001
Spring	25.6	20.8	27.9	32.3	24.1	1.09	0.22
Summer	12.0	7.9	34.6	19.5	21.4	0.55	<0.001

The data for BIP, BP, AIP, O-BRD, and other diagnoses (non-BRD) are shown; gross diagnoses of viral pneumonia (n = 18) are not included. The OR and P values compare BIP with other diagnoses.
Abbreviations: BIP, bronchopneumonia with interstitial pneumonia; BP, bronchopneumonia; AIP, acute interstitial pneumonia; O-BRD, other bovine respiratory disease; OR, odds ratio; IQR, interquartile range; n/a, not applicable.

.48), but median body weight at death was lower in BIP versus AIP cases (318 kg vs 465 kg; $P < .001$; Fig. 3b), and BIP cases spent less time in the feedlot prior to death (101 days vs 180 days; $P < .001$; Fig. 3c). BIP cases had a lower daily weight gain than AIP cases (0.61 kg/day vs 1.12 kg/day; $P < .001$). The time from the first clinical illness to death was longer for BIP versus AIP (19 days vs 1 day; $P < .001$; Fig. 3d), and more BIP cases had ≥2 separate instances of clinical illness prior to death (49.9% vs 27.3%; $P < .001$; Fig. 3e). BIP cases (compared with AIP cases) were more common in winter (48.2% vs 24.0%) and fall (14.1% vs 13.4%) and less common in spring (25.6% vs 27.9%) and summer (12.0% vs 34.6%; $P < .001$ across all 4 seasons; Fig. 3f). Two peaks in AIP frequency occurred (typically February to March and July to August), with the winter peak corresponding to that of BIP (Fig. 4; Supplemental Figs. S3–S6, Supplemental Tables S3–S5). Comparisons to O-BRD and non-BRD groups are shown in Table 1.

A logistic regression model using these descriptive variables identified factors associated with the probability of BIP death. The variables with the greatest predictive value were the number of clinical illnesses prior to death (0, 1, 2, 3, or ≥4 instances), the season of death (winter and spring), and animal weight upon arrival to the feedlot and at death (Supplemental Table S2 and Figs. S1 and S2). Specifically, the probability of diagnosing BIP was increased >12-fold if the animal had ≥4 instances of illness ($P < .001$) and was increased >3-fold if death occurred in winter ($P < .001$). Finally, every additional kilogram of body weight at arrival and at death reduced the odds of being diagnosed with BIP.

Validation Data Set

A population of 55 cases with diagnoses based on both gross and histopathology was used to validate the results of the primary data set. Summarized data for the primary and validation data sets are compared in Supplemental Table S1. Similar to the primary data set, the 18 BIP cases in the validation data set were predominantly steers (n = 14) with fewer heifers (n = 4),

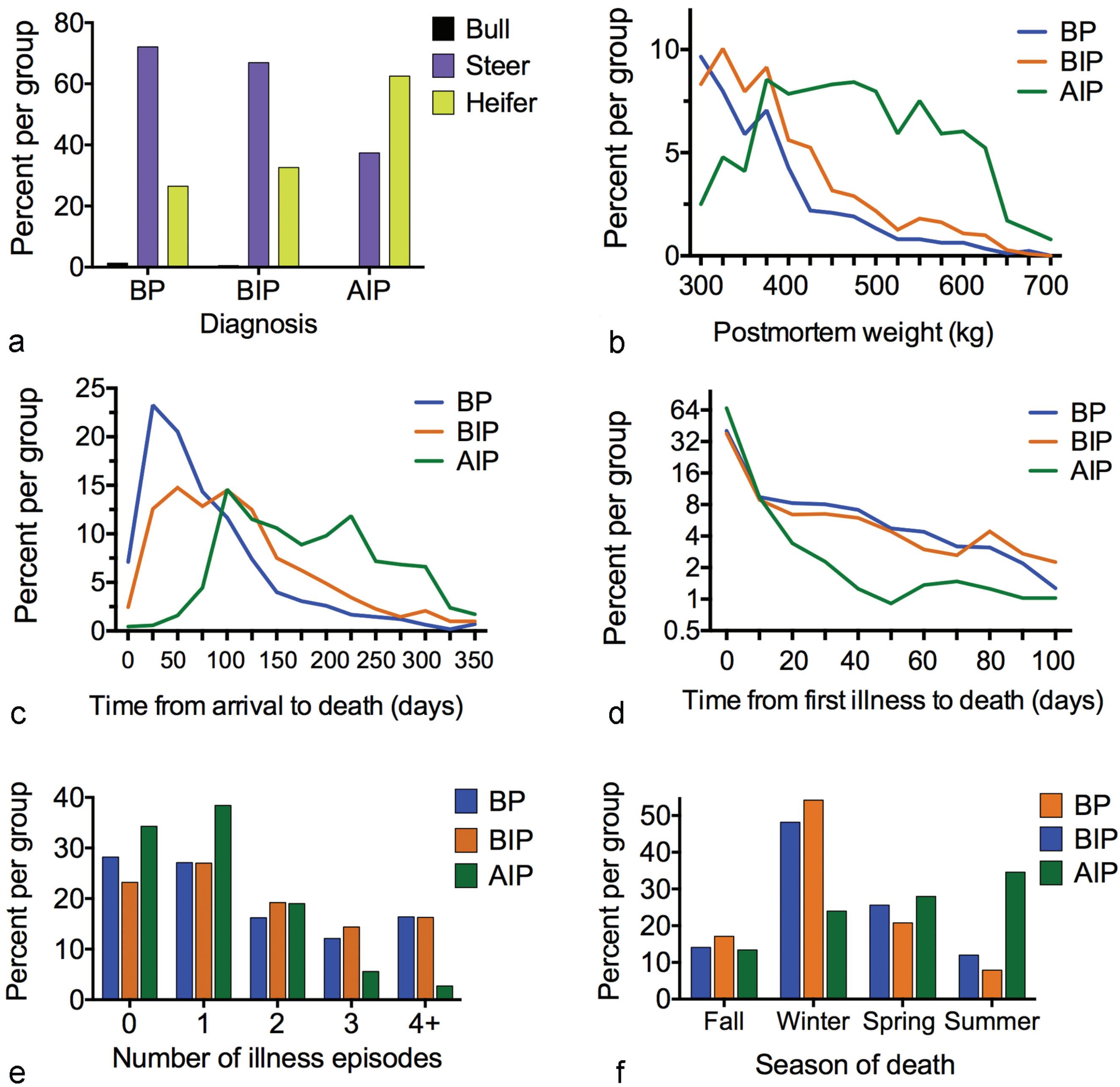

Figure 3. Comparison of cattle with postmortem diagnoses of bronchopneumonia (BP, n = 1729), bronchopneumonia with interstitial pneumonia (BIP, n = 1105), and acute interstitial pneumonia (AIP, n = 878), with respect to the distribution of (a) sex, (b) postmortem weights, (c) time between arrival to the feedlot and death, (d) time from the first clinical illness to death (note the y-axis $\log_2$ scale to show differences among groups), (e) number of separate instances of clinical illness, and (f) season in which the death occurred. The data show the percentage of cases for each diagnosis.

and most deaths occurred in winter (n = 8) or spring (n = 8) with fewer in summer (n = 1) or fall (n = 1). BIP cases spent a mean of 127 days in the feedlot prior to death. The average time from the onset of clinical signs to death was 55 days, and most had ≥1 instances of clinical illness prior to death (2 cases had no illness prior to death, 5 had 1 instance, 2 had 2 instances, 3 had 3 instances, and 6 had 4 instances of clinical illness).

Comparing BIP with BP cases, the validation data set was similar to the primary data set, in that BIP cases had higher body weights at death (349 kg vs 287 kg; P = .021), were in the feedlot longer before death (127 days vs 89 days; P = .023), and had a higher average daily weight gain (0.45 kg/day vs 0.09 kg/day; P = .013) than BP cases. BIP cases also had a trend to lower arrival body weights (258 kg vs 276 kg; P =

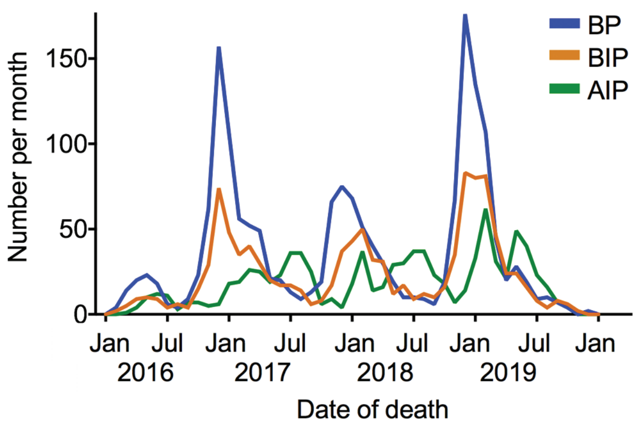

Figure 4. Frequency of mortalities by month in cattle with postmortem diagnoses of bronchopneumonia (BP, n = 1729), bronchopneumonia with interstitial pneumonia (BIP, n = 1105), and acute interstitial pneumonia (AIP, n = 878). BP deaths were most frequent in December. BIP was most frequent in February (or December, in 2017). AIP frequency showed 2 peaks: the first in February to March usually corresponding to the peak of BIP frequency, and a second peak in July to August (or May, in 2019).

.091). However, unlike the primary data set, BIP cases (compared with BP cases) in the validation data set did not have a lower proportion of steers (78% vs 71%), a longer time from the first clinical illness to death (55 days vs 54 days; P = .99), or a greater frequency of having ≥2 instances of clinical illness prior to death (61% vs 58%; P = .86; Supplemental Table S1).

Comparing BIP with AIP cases, the validation data set was similar to the primary data set, in that BIP cases had a lower proportion of heifers (22% vs 69%) and a higher proportion of steers (78% vs 31%; P = .009), similar mean body weights on arrival to the feedlot (258 kg vs 257 kg; P = .749), a nonsignificant tendency for lower mean body weights at death (349 kg vs 371 kg; P = .47), and lower average daily gain (0.45 kg/day vs 1.00 kg/day; P = .045) compared with AIP cases. BIP cases also had trends toward longer duration between the first clinical illness and death (55 days vs 22 days, P = .056) and to experience ≥2 instances of clinical illness prior to death (61% vs 30%; P = .095), compared with AIP cases. However, unlike the primary data set, BIP cases (compared with BP cases) in the validation data set did not have a shorter time in the feedlot before death (127 days vs 112 days; P = .40; Supplemental Table S1).

Discussion

This study described epidemiologic characteristics of feedlot cattle with pathologic diagnoses of BIP and compared these findings with those of BP and AIP. BIP was the second most frequent reason for death (or euthanasia) from respiratory disease, highlighting the disparity between the importance of the disease and the lack of knowledge of how it develops. Cattle dying of BIP were most likely to be steers rather than heifers, with a history of multiple episodes of clinical illness, poor weight gain, and death during winter typically 3–4 months after arrival to the feedlot. The frequency of BIP was twice that expected from chance concurrence of BP and AIP. BIP had many epidemiologic similarities to BP, whereas BIP differed from AIP in the sex distribution (steer predominance for BIP vs heifer predominance for AIP), seasonal distribution (winter and spring for BIP vs spring and summer for AIP), and other characteristics. Overall, the study results suggest that BIP is a distinct condition of feedlot cattle with differences from AIP, even though cranioventral and caudodorsal lung lesions of BIP are pathologically and microbiologically similar to those of BP and AIP, respectively.[4]

A goal of the study was to determine if BIP is a unique disease entity or merely a chance concurrence of BP and AIP in the same animal. The observed frequency of BIP cases in this study population was about 2-fold greater than that expected to arise by chance. Because our previous study identified that, in BIP cases, the cranioventral lesions of BP were older than the caudodorsal lesions of alveolar and bronchiolar damage (a form of interstitial/bronchointerstitial lung disease),[4] this finding suggests that chronic BP might predispose these calves to developing acutely fatal interstitial lung disease.[4,8,11]

This study identified differences between BIP and AIP which additionally support that they are distinct conditions. Whereas AIP cases had a consistent heifer predominance in this study and prior studies,[1,6,7,12,15] BIP cases more often affected steers. In this and previous reports,[14] AIP typically affected well-conditioned cattle with favorable growth characteristics, late in the feeding period, whereas BIP cases in this study had lower daily weight gains and spent less time in the feedlot prior to death compared with AIP cases. Animals dying of AIP are usually previously healthy animals with a sudden or unexpected onset of clinical disease that is unamenable to therapy and progresses rapidly to death within days of onset.[14] In this study, half of the BIP cases had ≥2 prior instances of clinical illness, whereas most AIP cases had ≤1 instance of prior illness, and the duration from the first clinical illness to death was longer for BIP than AIP cases.

Deaths from AIP were most common in the summer, whereas deaths from BIP were most common in winter. The occurrence of AIP in the summer has been associated with hot and dusty conditions, although it remains unknown if these environmental conditions play a causal role in pathogenesis.[1,6,14] By contrast, the predominance of BIP deaths in winter parallels the timing of BP deaths, consistent with the idea that chronic BP plays a role in progression to BIP. The large number of cases in this study allowed identification of 2 peaks of AIP frequency, 1 with a lower proportion of heifers in February to March coinciding with the highest BIP frequency and soon after the peak BP frequency, and a second peak of AIP frequency with a higher proportion of heifers that was typically in July to August. This might suggest that, in a population at risk of AIP because of exposure to the unknown causal agent (such as elevated blood levels of a lung toxicant), different factors may tend to trigger the progression to interstitial lung damage in steers versus heifers and in winter versus summer.

Specifically, because the prevalence of BP is higher in steers than in heifers, chronic clinical or subclinical BP might be more likely to promote the development of interstitial lung damage in at-risk steers in the winter. Conversely, because the increased risk of AIP in heifers is well known although the biological mechanism is unclear,[7,10,12] other sex-associated factors such as endogenous or exogenous female sex hormones may promote this progression in heifers. Thus, the differences in sex ratios, seasonal occurrence, number of prior clinical illnesses, days on feed at the time of death, and weight gain documented in this study may help clinicians and pathologists distinguish animals with AIP from those with BIP, but these dissimilarities also highlight the distinct nature of the 2 diseases and offer clues about pathogenesis.

In comparison with the other diagnoses, epidemiologic features of BIP most closely resembled those of BP in this study. Several variables had subtle albeit statistically significant differences between these groups, including sex distribution (more heifers for BIP vs BP), body weight upon arrival to the feedlot (lower for BIP), number of instances of clinical illness prior to death (more instances of illness for BIP), and seasonal distribution (BP was most frequent in fall and winter; BIP in winter and spring). However, the small magnitude of the differences may not be useful for clinically distinguishing these conditions. BIP cases became more frequent slightly later in winter than BP cases and continued into spring (when BP was less frequent), consistent with BIP cases having a longer time from the first clinical illness to death compared with BP cases. Larger average differences that might be clinically detected were that BIP cases spent >1 month longer in the feedlot before death, lived 1.36-fold longer after their first instance of clinical illness, and had >5-fold higher daily weight gains (despite poor growth compared with other groups) compared with BP cases. These differences probably reflect differences reported in our prior study, that BP cases tend to die of more acute disease associated with more virulent bacteria (ie, *M. haemolytica* genotype 2), whereas BIP cases tend to have a chronic relapsing or progressive clinical illness associated with secondary or less virulent bacteria.[4] For example, calves that were never infected with *M. haemolytica* genotype 2 or that cleared this more virulent pathogen may progress to chronic bronchopneumonia associated with less virulent opportunistic pathogens, and we speculate that this prolonged survival with chronic lung inflammation might predispose to an acutely fatal episode of alveolar and bronchiolar damage. For example, it has been speculated that chronic lung inflammation might alter metabolism of a lung toxicant and thus increase the risk of lung injury.[2,4]

Nonetheless, many BP cases also have a prolonged or relapsing clinical course. This, along with evidence that the cranioventral lung lesion is morphologically similar and not more extensive in BP versus BIP,[4] implies that chronic BP is not the only determinant of whether caudodorsal interstitial lung damage develops in animals with BP. For example, factors promoting exposure to or absorption or metabolism of a feed-derived lung toxicant may also be required.

The logistic regression model comparing BIP cases with all other causes of death also identified that the most significant predictors of a postmortem diagnosis of BIP were the number of instances of clinical illness, the season in which death occurred, and body weights at arrival to the feedlot and at death. The number of instances of clinical illness was a particularly strong predictor of BIP. When controlling for other variables and compared with animals dying with no instances of illness, animals with ≥4, ≥3, ≥2, or ≥1 prior illnesses had a 12.5-, 10.8-, 7.3-, and 3.2-fold increase in the probability of a postmortem diagnosis of BIP, respectively. Similarly, death in winter conferred a 2.98-fold increase in the likelihood of postmortem diagnosis of BIP. Lower arrival weights and postmortem weights were associated with an increased likelihood of a postmortem diagnosis of BIP, and although the odds ratio was only 0.998 (per kilogram of body weight change), the cumulative predictive effect was still substantial across a wide range of body weights. Finally, the logistic regression model identified an interaction between the number of instances of clinical illness and the season in which the animal died, which was attributed to the higher number of BP versus BIP cases in fall and winter (Supplemental Table S2—Supplemental Note).

Caveats in this study are that some postmortem weights were estimated by feedlot staff, and that the number of clinical illnesses and the time from the first clinical illness to death depend on subjective clinical recognition of sick calves which could introduce differential bias if some diseases were more clinically apparent than others. Diagnoses in the primary data set (9909 cases) were based on gross postmortem examination, and diagnoses were made by multiple veterinarians, thus introducing potential misclassification bias because gross diagnosis was previously shown to have 83% sensitivity and 73% specificity relative to histopathology.[4] For this reason, the smaller validation data set (55 cases) was analyzed to evaluate if the diagnostic method substantially affected the main findings of the study. It should be noted that this validation population was not a random sample of the feedlot population, as these 55 cases tended to be sampled in winter (which would affect the seasonal distribution of diagnoses), and the smaller size of the population resulted in lower statistical significance for many variables. Nonetheless, most variables that differentiated BIP from the other 2 disease groups showed the same trends or remained significant in the validation data set (Supplemental Table S1), thus supporting the findings from the primary data set.

Conclusions

BIP is a disease of feedlot cattle diagnosed based on pathologic findings of BP in the cranioventral lung and interstitial lung damage in the caudodorsal lung. Many characteristics of BIP resemble those of BP, except that BIP cases tend to have more chronic or relapsing clinical histories. Importantly, BIP is epidemiologically distinct from AIP. AIP is generally an acutely progressive disease of previously healthy, fast-growing, well-conditioned heifers, relatively late in the feeding period and most common in the summer months. In contrast, BIP cases typically have chronic and recurrent episodes of clinical illness associated with reduced weight gains, more commonly affect steers than heifers, and have usually been in the feedlot for 3–4 months prior to their death in the late winter to early spring. These differences from AIP, and the fact that BIP frequency in this study population was about twice what is expected by chance concurrence of BP and AIP, define BIP as being a distinct condition. These epidemiologic differences between BIP and AIP suggest that in cattle at risk of IP, female sex-specific factors may promote progression to AIP, whereas chronic infection of the lung with less virulent or secondary bacterial pathogens[4] may promote progression to BIP.

Acknowledgments

The authors thank the staff and clients of Feedlot Health Management Services for procuring samples and data.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This work was supported by the Beef Cattle Research Council of the Canadian Cattleman's Association (grant no. ANH 13.17), the Natural Sciences and Engineering Research Council of Canada (grant nos. NSERC; RGPIN-2017-03872; RGPAS-2017-507803), Beef Farmers of Ontario (grant no. 20-1679), and the Ontario Ministry of Agriculture, Food and Rural Affairs through the Ontario Agri-Food Innovation Alliance (grant no. UG-T1-2020-100075).

ORCID iDs

Luke A. J. Haydock https://orcid.org/0000-0002-3776-6654
Jeff L. Caswell https://orcid.org/0000-0002-1991-3219

References

1. Ayroud M, Popp JD, VanderKop MA, et al. Characterization of acute interstitial pneumonia in cattle in southern Alberta feedyards. *Can Vet J*. 2000;**41**(7):547–554.
2. Curtis RA, Thomson RG, Sandals WC. Atypical interstitial pneumonia in cattle. *Can Vet J*. 1979;**20**(5):141–142.
3. Haydock L, Fenton RK, Sergejewich L, et al. Acute interstitial pneumonia and the biology of 3-methylindole in feedlot cattle. *Anim Health Res Rev*. 2022;**23**(1):72–81.
4. Haydock LA, Fenton RK, Veldhuizen RAW, et al. Bronchopneumonia with interstitial pneumonia in beef feedlot cattle: characterization and laboratory investigation. *Vet Pathol*. 2023;**60**(2):214–225.
5. Hjerpe CA. Clinical management of respiratory disease in feedlot cattle. *Vet Clin North Am Large Anim Pract*. 1983;**5**(1):119–142.
6. Jensen R, Pierson RE, Braddy PM, et al. Atypical interstitial pneumonia in yearling feedlot cattle. *J Am Vet Med Assoc*. 1976;**169**(5):507–510.
7. Loneragan GH, Gould DH, Mason GL, et al. Association of 3-methyleneindolenine, a toxic metabolite of 3-methylindole, with acute interstitial pneumonia in feedlot cattle. *Am J Vet Res*. 2001;**62**(10):1525–1530.
8. Loneragan GH, Gould DH, Mason GL, et al. Involvement of microbial respiratory pathogens in acute interstitial pneumonia in feedlot cattle. *Am J Vet Res*. 2001;**62**(10):1519–1524.
9. Panciera RJ, Confer AW. Pathogenesis and pathology of bovine pneumonia. *Vet Clin North Am Food Anim Pract*. 2010;**26**(2):191–214.
10. Popp JD, McAllister TA, Kastelic JP, et al. Effect of melengestrol acetate on development of 3-methylindole-induced pulmonary edema and emphysema in sheep. *Can J Vet Res*. 1998;**62**(4):268–274.
11. Sorden SD, Kerr RW, Janzen ED. Interstitial pneumonia in feedlot cattle: concurrent lesions and lack of immunohistochemical evidence for bovine respiratory syncytial virus infection. *J Vet Diagn Invest*. 2000;**12**(6):510–517.
12. Stanford K, McAllister TA, Ayroud M, et al. Effect of dietary melengestrol acetate on the incidence of acute interstitial pneumonia in feedlot heifers. *Can J Vet Res*. 2006;**70**(3):218–225.
13. US Department of Agriculture. Feedlot 2011 Part IV: health and health management on U.S. feedlots with a capacity of 1,000 or more head. 2013. https://www.aphis.usda.gov/animal_health/nahms/feedlot/downloads/feedlot2011/Feed11_dr_PartIV_1.pdf
14. Woolums AR. Feedlot acute interstitial pneumonia. *Vet Clin North Am Food Anim Pract*. 2015;**31**(3):381–389, vi.
15. Woolums AR, Mason GL, Hawkins LL, et al. Microbiologic findings in feedlot cattle with acute interstitial pneumonia. *Am J Vet Res*. 2004;**65**(11):1525–1532.