Original Research Paper

Pathologies of Acute Interstitial Pneumonia in Feedlot Cattle

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Abstract: Acute Interstitial Pneumonia (AIP) is a costly issue that affects feedlot cattle. Research has yet to elucidate the etiology of AIP; therefore a case-control study was conducted to evaluate possible management and physiological factors that contribute to AIP in feedlot cattle. The experiment was conducted during the summer of 2011 in a commercial feedyard in Kansas. Animals exhibiting clinical signs of AIP and a control animal from the same pen were selected for ante-mortem examination. Post-mortem AIP cases were also selected for additional examination. Ante-mortem measurements included rumen gas cap hydrogen sulfide and pH, rectal temperature and body weight. Post-mortem examination added histological examination of lung tissue. Rectal temperature was greater in the AIP cattle (40.6±0.16°C) than controls (39.7±0.16°C; $p<0.001$). Body weight (499±56 Vs. 506±60 kg), hydrogen sulfide (136±133 vs. 269.8±311 ppm) and rumen pH (6.4±0.5 Vs. 6.2±0.6) were similar between AIP and control cattle ($p>0.10$). Post-mortem rumen pH values were 6.3±0.4 and 5.7±0.6 for AIP and control cattle, respectively. Histological evaluation of lung samples showed that bronchiolitis was present in about 90% of the cattle affected with AIP. About 75% of the cattle with AIP also had bronchopneumonia. No relationships between feed intake patterns, or serum amylase or lipase levels were noted between treatments ($p>0.20$). This study generally confirms that AIP tends to occur more in heifers relative to steers, occurs in cattle at heavier weights or later in the feeding period and tends to be associated pathologically with bronchio` litis and bronchopneumonia. The lack of differences in rumen measures and the feed intake data between AIP and control cattle suggest that feed intake patterns and rumen fermentation may not impact AIP in feedlot cattle and that it may be more directly related to bronchiolitis/bronchopneumonia due to chronic irritation or infection.

Keywords: Acute Interstitial Pneumonia, Feedlot Cattle, Lung Lesions

Introduction

Acute Interstitial Pneumonia (AIP) is a respiratory disease that affects feedlot cattle, especially during dry and hot weather patterns (Woolums *et al*., 2005a). This disease is also known as atypical interstitial pneumonia, fog fever and dust pneumonia (Woolums *et al*., 2005b). Following Bovine Respiratory Disease (BRD), AIP is one of the most costly diseases confronted by feedlots (Amosson *et al*., 2006). It tends to affect cattle that are near to their market weight and in addition to the loss of the animal, economic costs include the value of a large amount of feed, yardage, interest and any other investments in the animal (Loneragan *et al*., 2001b). In 2000, the National Animal Health Monitoring System reported that 78.4% of all feedlots had at least one animal develop AIP (NAHMS, 2000b). A survey of U.S. feedlot personnel estimated that 3.1% of the total cattle placed on feed develop AIP (NAHMS, 2000a).

Cattle affected by AIP develop clinical signs such as extension of the neck to facilitate breathing, excessive salivation, grunting, panting, breathing through the mouth and refusal to travel (Blood, 1962; Doster, 2010). Affected animals also may express aggressive attitudes when being approached for handling (Loneragan and Gould, 1999). Cattle that display AIP-like symptoms tend to respond poorly to treatments (Woolums *et al*., 2005b). At necropsy, lungs grossly display edema and emphysema (Doster, 2010). Even though it is a very costly disease, research has yet to elucidate the exact etiology of AIP in feedlot cattle. Factors such as heat stress, dust exposure, viruses, feed toxins, toxic gasses such as hydrogen sulfide produced in the rumen, gender, parasites and several other factors have been associated with AIP (Sorden *et al*., 2000; Doster, 2010). Feedlot veterinarians have speculated that pancreatitis may be involved with AIP. Hydrogen sulfide has been shown to cause lung lesions in rats (Lopez *et al*., 1987; Prior *et al*., 1988). Also in grazing cattle, AIP been tied to the L-tryptophan content of lush forages and the resulting 3-methylindole metabolism in the rumen (Loneragan *et al*., 2001a). This study was conducted to clinically observe ante-mortem cases of cattle suffering from AIP compared to their non-affected pen cohorts and examine management conditions or cattle feeding behavior that might lead to AIP incidence in cattle feeding facilities. Also, an objective of this study was to assess the gross and histological pathology of cattle that died due to AIP to better understand the pathenogenesis of the disease.

Materials and Methods

Cattle

All procedures in the study were approved by the Institutional Animal Care and Use Committee at Kansas State University (No. 3044).

The study was conducted in a commercial feedlot with a capacity of approximately 55,000 head in southwest Kansas during the summer of 2011. The cattle population demographics consisted of 75% heifers and 50% black-hided animals. Average body weight at arrival of cattle was 354 kg. At initiation of the study the cattle ranged from 3 to 166 Days On Feed (DOF) with an average of 64 DOF. The finishing diet was about 44% flaked corn, 20% high moisture corn, 22% wet distillers grains, 3.7% dry distillers grains, 5.1% ground corn stalks and 5.1% liquid supplement on a dry matter basis. Feed consumption data were obtained from the feedlot records.

Case animals suspected of AIP were identified ante-mortem based on clinical signs, which included: extension of the neck, panting, excessive salivation, breathing through the mouth and refusal to travel (Blood, 1962; Doster, 2010). Suspect animals were removed from their pen and taken to the hospital facilities for examination or were collected in the home pen if the animal was unable to rise. Animals diagnosed with AIP (case) were paired with a healthy control animal of comparable physical characteristics from the same pen. At the time of sample collection, the date, sex, lot and tag number and hide color were recorded. All sample collections were performed by a Kansas State University graduate student and properly trained personnel from the feedlot hospital crew.

Samples

In both case and control animals, samples from the rumen gas cap were collected using a rumen puncturing technique (Kleen *et al*., 2004). A total of 200 mL of rumen gas was collected for measurement of H_2S (100 mL per gas measured). Rumen hydrogen sulfide levels were determined using 2 detector tubes with different detection ranges (Gastec Corporation, Ayase-shi, Kanagawa, Japan). Hydrogen sulfide samples initially used a [C]NO.4H tube which had a range of 100 to 2,000 ppm. If the amount of H_2S exceeded the scale range, a second 100 mL sample was taken using a [D]NO.4HH tube with a 0.1 to 2.0% scale range. Rumen fluid was obtained following a rumen sampling procedure similar to the technique used to collect the rumen gas samples. A 12-gauge needle was introduced into the rumen on the left side of the animal just caudal to the 13^{th} rib at the level of the point of the elbow. At least 6 mL of rumen fluid was obtained to measure the rumen pH.

Blood samples were obtained for serum chemistry analysis. Approximately 12 mL of blood was obtained from the jugular vein and divided into 2 aliquots of 6 mL each, allowed to clot, centrifuged and refrigerated. The samples were then shipped for laboratory analysis of amylase and lipase contents (IDEXX Laboratories, Westbrook, Maine) to observe pancreatitis as a possible cause for acute lung injury as evidenced in human medicine (Zhou *et al*., 2010).

Rectal temperature was determined using an electronic digital thermometer. Body weight was recorded in the hospital chute for those animals receiving an ante-mortem examination. The weights for the animals receiving a post-mortem examination but without an ante-mortem examination that died in their home pen were estimated using their home penmate's weight average.

Post-mortem examination was performed on suspected AIP mortalities independent of whether they had received an ante-mortem examination. Post-mortem case animals were confirmed based on lung histopathology. At the time of necropsy, post-mortem controls were selected from animals that were suspected of dying of causes other than AIP. Post-mortem AIP suspects and controls were paired by the best match of the animal's demographic information (sex, weight, home pen). Throughout the study, necropsies were performed by experienced personnel trained by the feedyard consulting veterinarian. Only animals suspected of AIP that died early in the morning and showed no signs of physical decomposition were examined.

Rumen gas-cap samples were obtained at necropsy following the same technique as the ante-mortem examination, except that the rumen was exposed. Rumen pH was collected by making a small incision in the rumen wall to insert the pH meter into the rumen liquor.

Lung tissue samples were obtained by a single trained person. Samples (4 total lung samples for each animal) were collected from lung lobes with consolidated tissue. In the majority of animals, the caudal lobe contained consolidated tissue and was the site of sample collection. Samples were collected along lines demarcation between consolidated and non-consolidated tissue so that each sample contained both types of tissue. Tissues were sectioned in blocks of similar dimensions (approximately 6.35 cm length x 1.9 cm width x 1.9 cm depth). Each sample was individually placed in formalin, labeled with the lot number, animal ID and lobe location. Formalin fixed-samples were stored in a room with no sunlight and at a temperature of approximately 21°C. Samples were shipped on a weekly basis to the Arizona Veterinary Diagnostic Laboratory at the University of Arizona for histopathology analysis.

Post-mortem, animals were classified AIP positive by presenting histopathological lesions such as alveolar fibrin, hyaline membrane formation and pneumocyte hyperplasia in at least one lobe (Sorden *et al*., 2000; Woolums *et al*., 2004). Histopathological lesions were further defined as focal AIP (less than 10% of lobule affected), patchy AIP (more than 10% but less than 50% of the lobule affected), diffuse AIP (more than 50% of the lobule affected), bronchopneumonia (focal or diffuse acute/chronic), chronic bronchopneumonia (broncho-pneumonia plus evidence of chronicity such as fibrosis or atelectasis), histopathological interstitial pneumonia (interstitial pneumonia lacking gross lesions described for AIP but having interstitial cellular or acellular interstitial infiltrates upon histopathological analysis). The presence of bronchopneumonia, bronchiolitis and interstitial pneumonia lesions were also evaluated.

Variation in 14-day feed consumption was compared in a case-control approach between pens with at least one case of AIP (n = 44) verses selected control pens with no reported cases of AIP. A second comparison in feed variation was made using a 5-day rolling average compared to the 6th day feed consumption. The control pen was selected based on sex, DOF, average weight, number of cattle in the pen and location within the feedlot. For statistical analysis, dry matter intake variations were categorized as the number of pens varying from the previous day or the rolling average by $\geq$0.11, 0.23, or 0.34 kg·animal^{-1}·day^{-1}.

Ambient temperature and humidity at the feedlot location were automatically recorded by a central station and a weather censor located on site. Samples collection was conducted from June 10 to August 10, 2011. High and low daily temperatures were graphed with the daily incidence of AIP in cattle.

Statistical Analysis

The experimental design was a case-control study to evaluate possible factors contributing to AIP in feedlot production settings. A *P* value $\leq$0.05 was selected to establish statistical significance among evaluations. Probability values >0.05 but $\leq$0.1 were described as values approaching statistical significance. Ante-mortem observations of rectal temperature, weight, rumen H_2S and rumen pH were analyzed using a mixed-effects model analysis of variance (SAS Institute, Inc. Cary, NC) with ante-mortem classification as a fixed effect and with sex and pairing as random effects. Means were separated using the PDIFF option of SAS. This ante-mortem analysis focused on 23 pairs of AIP affected animals and controls.

Ante-mortem observations of serum amylase and lipase demonstrated biphasic distributions of zero and positive values and therefore, were evaluated using a Wilcoxon Ranked Sum procedure in SAS. The number of cattle in the various ante and post-mortem examination groups varied. Due to the large differences in numbers and the lack of histological confirmation of control animal lung pathology, serum amylase and lipase were reported but not statistically evaluated.

Feed consumption changes were analyzed using the Proc Mixed procedure to compare the pens with AIP cases to control pens without AIP cases. Pen classification, with or without an AIP case, was a fixed effect and no random effects were included in the model.

Results

The number of animals in the various ante-mortem and post-mortem groups are shown in Table 1. In this study, AIP affected cattle from 24 to 131 DOF and at an average body weight of 505 kg.

Ante-Mortem

A total of 31 animals were diagnosed with AIP and received an ante-mortem examination. Serum chemistry was completed on 30 animals. Eighty-seven percent were heifers compared to the estimated heifer percentage in the feedlot of 75%. Hide colors for the 31 animals were 74% black, 16% red and 10% white.

Twenty-three case controls were examined ante-mortem. Live weights were similar between the two groups (499±56 Vs. 506±60 kg). Sixteen of the 31 animals with ante-mortem examination also received a post-mortem examination.

The remaining 14 animals were in an advanced state of decomposition and necropsies were not performed. In addition, 44 possible AIP cases that died prior to the opportunity for an ante-mortem received post-mortem examination. Eleven post-mortem cattle that died from obviously non-AIP causes were selected as controls at the time of necropsy. A total of 71 cattle received post-mortem examination.

Table 1. Animal numbers in the various ante-mortem and post-mortem groups

	Identified Ante-mortem		Identified Post-mortem	
Item	Ante-mortem examination	Post-mortem examination	Post-mortem examination	Lung examinations
AIP[a] suspect	31	16	44	60
Control	23	0	11	0
Lung histology				
AIP confirmed		13	32	45
Bronchiolitis		15	40	55
Bronchopneumonia		10	24	34

[a]Acute interstitial pneumonia

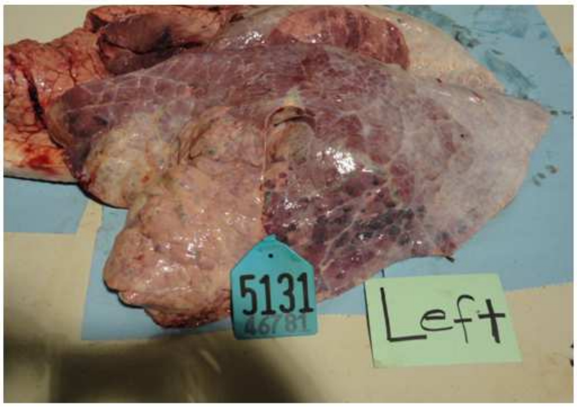

Fig. 1. Example of lung showing gross AIP lesions

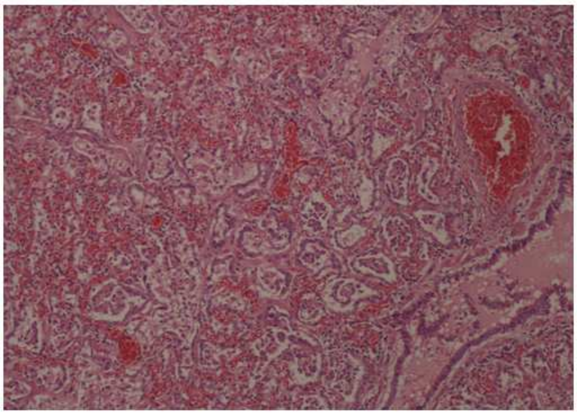

Fig. 2. Image of diffuse AIP lung lesions

In the ant-mortem examinations, there were no differences (P = 0.99) in serum amylase or lipase concentrations, indicators of pancreas function, between control animals and AIP suspects (Table 2). Suspected AIP cases had numerically lower ($P = 0.09$) rumen gas cap hydrogen sulfide concentration (H_2S; 110±68) than the control group (273±59; Table 2). Rumen pH values among the control and the AIP suspect groups approached significance ($P = 0.06$, Table 2). Cattle suspected of AIP had greater ($p<0.0001$) rectal temperature (40.6±0.16°C) than the control animals (39.7±0.16°C). There were no differences in body weights between the control cattle and the AIP suspect cattle ($P = 0.22$).

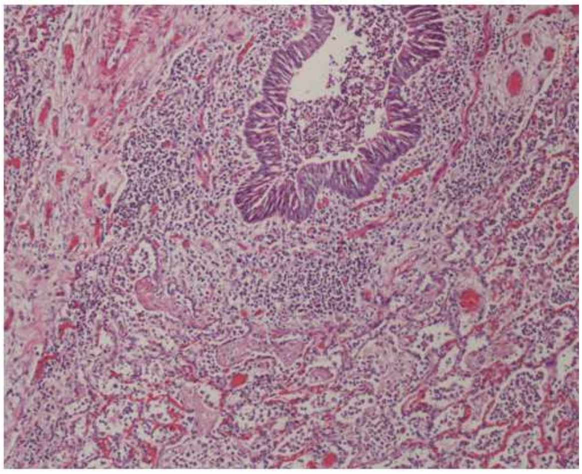

Fig. 3. Image of focal AIP lesions around bronchioles

Post-Mortem

Lung samples from 60 animals were submitted to the laboratory. Diffuse, focal and patchy AIP lesions were present in 45 of the 60 animals at levels that met the criteria for AIP diagnosis (Fig. 1). Single type lung lesions diagnosed 15 animals with AIP (5, 6 and 9 for diffuse (Fig. 2), focal (Fig. 3) and patchy, respectively) and 30 animals had more than one type of lesion present. In addition, AIP lesions were present in 10 animals but at less than 10% of lobule. Bronchopneumonia was confirmed to be present in 34 of the 60 animals. Fifty-five of the 60 had lesions consistent with bronchiolitis.

In the post-mortem examinations, rumen pH values of the 60 AIP animals were numerically greater than the values obtained from 11 control animals, 6.3±0.4 and 5.7±0.6, respectively. Cattle with AIP also had numerically lower H_2S concentration (1,280 ppm) than the control group (1,841 ppm). Statistical significance between the AIP and control groups was not calculated for the rumen pH or hydrogen sulfide due to the lack of lung histology of the control group.

Ante- and Post-Mortem

Sixteen animals had both ante-mortem and post-mortem examinations; 13 (81%) had diffuse, focal and patchy AIP confirmed by histology.

Table 2. Average ante-mortem rectal temperature, rumen hydrogen sulfide (H_2S), rumen pH, and serum amylase and lipase for Control and cattle diagnosed with Acute Interstitial Pneumonia (AIP)

Treatment	N	Rectal temp., ^0F	Rumen H_2S, ppm	Rumen pH	Amylase, U/L	Lipase, U/L
Control	30	103.5	273	5.9	8.9	11.2
AIP[a]	23	105.4	110	6.2	8.7	11.1
SEM		0.30	68	0.3	2.4	5.8
P value		< 0.001	0.09	0.06	0.99	0.99

[a] Acute interstitial pneumonia

Table 3. Number of pens with changes in feed consumption volume during the 14 days prior to Acute Interstitial Pneumonia (AIP) incidence

	Number of pens			
Change kg·animal^{-1}·day^{-1}	Control	AIP	SEM	P value
> 0.11	8.3	7.7	0.3	0.03
> 0.23	5.5	5.3	0.4	0.62
> 0.34	3.7	3.6	0.3	0.88

Table 4. Number of pens with changes in 5-day rolling average of feed consumption prior to Acute Interstitial Pneumonia (AIP) incidence

	Number of pens			
Change kg·animal^{-1}·day^{-1}	Control	AIP	SEM	P value
> 0.11	3.1	2.7	0.2	0.13
> 0.23	2.0	1.8	0.2	0.59
> 0.34	1.4	1.0	0.2	0.15

Acute and chronic bronchiolitis lesions were found in 12 of the 13 animals with AIP and in the 3 animals with no histological AIP lesions. Of the 16 animals, 10 (63%) had some form of bronchopneumonia.

Weather and Feed Patternsi

High and low daily temperatures were gathered from the weather station for a graphical analysis in comparison with the daily incidence of AIP in cattle. No association between temperature changes and the incidence of AIP was observed.

Comparisons of feed variations between the pens with at least one AIP incident during the time of the study and their assigned control pen were made. Feed variations were statistically evaluated between the AIP and control groups in ≥0.11, 0.23 and 0.34 kg/animal daily change. During both 14 (compared to the previous day) and 5 day (compared to the 5 d rolling average) periods prior to the AIP incidence, the number of pens with changes of ≥0.11, 0.5 and 0.34 kg·animal-1·day-1 did not differ between pens with and without AIP cases ($p = 0.13$ to 0.88). The results are shown in Tables 3 and 4.

Discussion

Acute interstitial pneumonia was found in a higher numeric proportion of heifers than would have been expected based on the proportion of heifers in the feedlot (75%). During the ante-mortem phase of this study, 87% of the animals suspected of AIP were heifers (n = 27) and during the post-mortem phase 96% of the cattle with AIP confirmed on histology were heifers. This numeric finding agrees with previous studies that reported feedlot heifers were more prone to be affected by AIP than steers. In a study conducted in southern Alberta feedyards, all the animals suspect of AIP were heifers even though the heifer to steer ratio during the time of the study was 8:1 (Ayroud *et al*., 2000). Woolums *et al*. (2001) also reported that heifers died of AIP at higher ratios than steers.

In this study, AIP affected cattle from 24 to 131 DOF and at an average body weight of 505 kg. Acute Interstitial Pneumonia has been reported in cattle as early as 45 d and to continue in cattle up to 15 to 45 d prior to expected slaughter date (Woolums *et al*., 2001; Stanford *et al*., 2006). In other studies, AIP was observed to be a prevalent cause of death in cattle that are nearing market weight (Jensen *et al*., 1976; Loneragan and Gould, 1999). In a nationwide survey evaluating the association between management practices and the risk of AIP, feedlot managers reported that about 80% of all the AIP deaths were in cattle that had been on feed for 60 days or more and averaged 24 d before expected slaughter date (Ayroud *et al*., 2000).

Acute Interstitial Pneumonia has been reported to affect cattle more commonly during hot and dry summers (Ayroud *et al*., 2000; Woolums *et al*., 2005a) or during the fall season (Hammond *et al*., 1979). It is possible that heat stress contributes to the incidence of

AIP. This study was conducted for about 60 d during the months of June, July and August. Cattle suspected of AIP were shown to have ($p<0.0001$) greater rectal temperature values (40.6±0.16°C) than the control animals (39.7±0.16°C). It is not possible to determine if the increased rectal temperature was an immune response, accumulated heat load, or caused by other factors.

At necropsy, animals suspected of AIP presented pulmonary characteristics such as enlarged lungs, dark red color, rubbery texture and interstitial edema and intralobular emphysema. These lesions were often diffusely distributed throughout the lung lobes. These observations were similar to gross lesions reported in previous studies (Curtis *et al*., 1979; Woolums *et al*., 2005b; Doster, 2010). Histological evaluation of lung samples showed that bronchiolitis lesions were present in more than 90% of the cattle affected with AIP. About 75% (34/45) of the cattle with AIP also had bronchopneumonia lesions. The percentage of AIP cattle with bronchopneumonia was in agreement with previous reports. In a study of feedlot-associated AIP, 97% of the cattle affected with AIP (n = 149) also presented evidence of bronchopneumonia (n = 144) (Hjerpe, 1983). In another study, 75% of the cattle with AIP (n = 28) also became affected with bronchopneumonia (n = 21) (Sorden *et al*., 2000).

Ante-mortem serum amylase, lipase and rumen pH did not differ between cattle diagnosed with AIP and those without AIP. Hydrogen sulfide has been shown to cause lung lesions in rats (Lopez *et al*., 1987; Prior *et al*., 1988). If rumen H_2S concentrations contribute to AIP, it would be reasonable to expect H_2S to be higher in cattle affected by AIP than control animals. However in this experiment, AIP animals had numerically lower concentrations of H_2S than the control animals. The post-mortem H_2S levels were about 8 times greater than the ante-mortem levels. Post-mortem rumen pH values were numerically greater in the 60 AIP animals than 11 control animals (6.3 Vs. 5.7, respectively), which agrees with previous reports (Miles *et al*., 1998).

Feed factors such as readily available L-tryptophan and disturbances in feed intake patterns have been suggested as factors that contribute to increased AIP incidence. Feedlot diets typically do not contain high levels of highly available protein and the amino acid L-tryptophan that can be present in lush forages. However, increased levels of breakdown products of L-tryptophan have been found in the lungs of feedlot cattle with AIP (Loneragan *et al*., 2001a). In this study, there were no differences in feed intake patterns between pens that experienced a case of AIP and those that did not.

Conclusion

This study generally confirms the observations that AIP tends to occur in heifers, late in the feeding period and tends to be associated with bronchiolitis and bronchopneumonia. Cattle suspected of AIP had greater rectal temperature values (40.6±0.16°C) than animals classified as controls (39.7±0.16°C). The lack of differences in rumen measures and the feed intake data between AIP and control cattle suggest that feed intake pattern and rumen fermentation may not impact AIP in feedlot cattle. Future AIP research topics include the complications of heat stress, dusty conditions and water availability. Also, there are currently few effective treatments.

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Author's Contributions

Jose E. Valles: Performed the animal study and collected samples, performed data analysis and prepared the initial manuscript.

Daniel U. Thomson, Michael D. Apley and Chris D. Reinhardt: Conceptualized the study and were responsible for experimental design and participated in preparation of the publication.

Steven J. Bartle: Participated in the data analysis and interpretation and drafted the final manuscript. All authors approved the final version of the manuscript for publication.

Ethics

The authors declare that they have no competing interests.

References

Amosson, S.H., B. Guerrero and L.K. Almas, 2006. Economic analysis of solid-set sprinklers to control dust in feedlots. Proceedings of the 38th Southern Agricultural Economics Association Annual Meeting, Feb. 5-8, Orlando, pp: 1-20.

Ayroud, M., J.D. Popp, M.A. VanderKop, G.S. Yost and D.M. Haines *et al*., 2000. Characterization of acute interstitial pneumonia in cattle in Southern Alberta feedyards. Can. Vet. J., 41: 547-554. PMID: 10907577

Blood, D.C., 1962. A typical interstitial pneumonia of cattle. Can. Vet. J., 3: 40-47.

Curtis, R.A., R.G. Thomson and W.C.D. Sandals, 1979. Atypical interstitial pneumonia in cattle. Can. Vet. J., 20: 141-142.

Doster, A.R., 2010. Bovine atypical interstitial pneumonia. Vet. Clin. North Am. Food Anim. Pract., 26: 395-407. DOI: 10.1016/j.cvfa.2010.03.002

Hammond, A.C., B.J. Bradley, M.T. Yokoyama, J.R. Carlson and E.O. Dickinson, 1979. 3-methylindole and naturally occurring acute bovine pulmonary edema and emphysema. Am. J. Vet. Res., 40: 1398-1401. PMID: 525860

Hjerpe, C.A., 1983. Clinical management of respiratory disease in feedlot cattle. Vet. Clin. North Am. Large Anim. Pract., 5: 119-142. PMID: 6351409

Jensen, R., R.E. Pierson, P.M. Braddy, D.A. Saari and L.H. Lauerman *et al*., 1976. Atypical interstitial pneumonia in yearling feedlot cattle. J. Am. Vet. Med. Assoc., 169: 507-510. PMID: 956028

Kleen, J.L., G.A. Hooijer, J. Rehage and J.P. Noordhuizen, 2004. Rumenocentesis (rumen puncture): A viable instrument in herd health diagnosis. Deutsche Tierärztliche Wochenschrift, 111: 458-462. PMID: 15648614

Loneragan, G. and D. Gould, 1999. Acute interstitial pneumonia in U.S. feedlots. Proc Acad Vet. Consultants Winter Meeting, pp: 1-6.

Loneragan, G.H., D.H. Gould, G.L. Mason, F.B. Garry and G.S. Yost *et al*., 2001a. Association of 3-methyleneindolenine, a toxic metabolite of 3-methylindole, with acute interstitial pneumonia in feedlot cattle. Am. J. Vet. Res., 62: 1525-1530. DOI: 10.2460/ajvr.2001.62.1525

Loneragan, G.H., D.H. Gould, G.L. Mason, F.B. Garry and G.S. Yost *et al*., 2001b. Involvement of microbial respiratory pathogens in acute interstitial pneumonia in feedlot cattle. Am. J. Vet. Res., 62: 1519-1524. DOI: 10.2460/ajvr.2001.62.1519

Lopez, A., M. Prior, S. Yong, M. Albassam and L.E. Lillie, 1987. Biochemical and cytologic alterations in the respiratory tract of rats exposed for 4 hours to hydrogen sulfide. Fundamental Applied Toxicol., 9: 753-762. DOI: 10.1016/0272-0590(87)90182-5

Miles, D.G., B.W. Hoffman, K.C. Rogers and J.E. Sears, 1998. Diagnosis of digestive deaths. J. Anim. Sci., 76: 320-322. PMID: 9464914

NAHMS, 2000a. Part II: Baseline reference of feedlot health and health management. USDA, APHIS, National Animal Health Monitoring System.

NAHMS, 2000b. Part III: Health management and biosecurity in the U.S. Feedlots. USDA, APHIS, National Animal Health Monitoring System.

Prior, M.G. A.K. Sharma, S. Yong and A. Lopez, 1988. Concentration-time interactions in hydrogen sulphide toxicity in rats. Can. J. Vet. Res., 52: 375-379. PMID: 3167719

Sorden, S.D., R.W. Kerr and E.D. Janzen, 2000. Interstitial pneumonia in feedlot cattle: Concurrent lesions and lack of immunohistochemical evidence for bovine respiratory syncytial virus infection. J. Vet. Diagnostic Invest., 12: 510-517. DOI: 10.1177/104063870001200604

Stanford, K., T.A. McAllister, M. Ayroud, T.M. Bray and G.S. Yost, 2006. Effect of dietary melengestrol acetate on the incidence of acute interstitial pneumonia in feedlot heifers. Can. J. Vet. Res., 70: 218-225. PMID: 16850945

Woolums, A.R., G.H. Loneragan, L.L. Hawkins and S.H. Williams, 2005a. A survey of the relationship between management practices and risk of acute interstitial pneumonia at US feedlots. Bov. Pract., 39: 125-133.

Woolums, A.R., G.H. Loneragan, S.M. Hawkins and S.H. Williams, 2005b. Baseline management pracitices and animal health data reported by the US feedlots to a survey regarding acute interstitial pneumonia. Bov. Pract., 39: 116-124.

Woolums, A.R., G.L. Mason, G.L. Hawkins, C.C. Brown and S.M. Williams *et al*., 2004. Microbiologic findings in feedlot cattle with acute interstitial pneumonia. Am. J. Vet. Res., 65: 1525-1532. DOI: 10.2460/ajvr.2004.65.1525

Woolums, A.R., S.M. McAllister, G.H. Loneragan and D.H. Gould, 2001. Etiology of acute interstial pneumonia in feedlot cattle: Noninfectious causes. Comp. Continuing Ed., 23: 86-93.

Zhou, M.T., C.S. Chen, B.C., Q.Y. Zhang and R. Andersson, 2010. Acute lung injury and ARDS in acute pancreatitis: Mechanisms and potential intervention. World J. Gastroenterol., 16: 2094-2099. DOI: 10.3748/wjg.v16.i17.2094