PEER REVIEWED

Case report – Peracute to acute fatal pneumonia in cattle caused by *Bibersteinia trehalosi*

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Abstract

Three outbreaks of peracute to acute pneumonia in cattle of varying ages and breeds were investigated. Death losses were high, and often occurred within 12-24 hours of the onset of clinical signs of illness, in spite of aggressive antimicrobial treatment. Gross necropsy examinations consistently showed greater lung involvement (>50%) than expected for the short course of the disease. In each case, the primary (or only) pathogen isolated was *Bibersteinia trehalosi*, a bacteria closely related to *Mannheimia hemolytica*, which has been commonly associated with acute disease in sheep and goats.

Key words: cattle, BRD, pneumonia, *Bibersteinia trehalosi*

Résumé

Trois flambées de pneumonie suraiguë à aiguë chez des bovins d'âge et de race variées ont fait l'objet d'une enquête. La mortalité était élevée, survenant souvent 12 à 24 heures après les premiers signes cliniques de la maladie, malgré un traitement antimicrobien dynamique. Une nécropsie primaire a révélé de façon systématique une infection des poumons plus importante que prévu (> 50%) au cours de cette maladie qui a progressé rapidement. Dans chaque cas, le principal (ou l'unique) agent pathogène isolé était *Bibersteinia trehalosi*, une bactérie étroitement apparentée à *Mannheimia hemolytica*, elle-même couramment associée à une grave maladie chez les ovins et les caprins.

Introduction

Over the past several years, a relatively new peracute bacterial pneumonia syndrome has been reported in cattle in the United States and Canada. *Bibersteinia trehalosi*, a bacterium more commonly associated with pneumonia and septicemia in sheep,[8,13] has been isolated from pneumonic lungs of affected cattle. Attending veterinarians report that pneumonia caused by *B. trehalosi* is refractory to treatment, although susceptibility testing often demonstrates the organism is sensitive to many commonly used antimicrobials. While the greater number of cases have been reported in adult dairy cattle, *B. trehalosi* has been cultured from pneumonic lungs of animals in all sectors of the cattle industry, including adult beef cattle.

Bibersteinia trehalosi was originally identified as *Pasteurella hemolytica* biotype T in 1959, and was reclassified as *Pasteurella trehalosi* in 1990.[1,2,13] In 2007, the bacterium was renamed *Bibersteinia trehalosi* after Ernest Berbstein, an early pioneer in *Pasteurella* typing.[1,2] Although a separate genus and species, *B. trehalosi* is closely related to *Mannheimia haemolytica*, and the two are virtually indistinguishable on routine culture or gross postmortem examination of pneumonia cases. Further sugar digestion tests of the bacterial isolate can separate and identify the bacterium. *M. haemolytica* cannot digest trehalose, while *B. trehalosi* can digest trehalose, but cannot digest catalase.[1]

B. trehalosi has been identified as a primary bacterial pathogen in sheep. The disease has been characterized as a peracute, fatal pneumonia and septicemia with death often occurring within six to eight hours following onset of clinical signs.[8,9,10,14] Gross pathology in affected sheep includes severe congestion and edema of the lungs, which is often accompanied by serosal hemorrhage.[8,9,10,14] Embolic spread of the organism to other organs has been reported.[14] A challenge model for studying the disease in sheep has been developed.[15]

Limited information has been published about pneumonia in cattle caused by *B. trehalosi*, and neither

the bacterium nor the syndrome are cited in a recent edition of a leading large animal medicine textbook.[17] Since 2007, the Animal Health Laboratory-Guelph has identified 12 pneumonia and six septicemia cases in cattle involving this organism.[12] In 2008, the University of California-Davis Diagnostic Laboratory reported that *B. trehalosi* was isolated from lungs of pneumonic dairy cattle more often than *P. multocida* and *Histophilus somni* (Figure 1).[3,4,5] These reports suggest that isolation of the bacteria from bovine pneumonia cases is not unusual.

This paper reports three outbreaks of acute, fatal pneumonia associated with isolation of *B. trehalosi* representative of cases investigated across the United States and in Canada by the authors (VSC, DAB).

Case 1

History

This case involved a well-managed dairy farm located in northern Wisconsin. The herd consisted of 310 non-registered Holstein lactating and dry cows housed in a free-stall barn. Cows were milked three times daily in a rapid-exit, parallel parlor system. The rolling 305-day average milk production at the time of the outbreak was 24,000 lb (10,900 kg). The average bulk-tank somatic cell count was 280,000 cells/mL.

Cows were fed a total mixed ration. One potentially confounding factor was the high level of mycotoxin in harvested and stored wet feeds on the dairy.[7] Some mold was observed in the feed by the owners, and the feed tested positive for aflatoxins by the local feed mill. In response to this concern, feed additives[a,b] were being utilized to prevent potential adverse effects associated with mycotoxins.

Clinical findings and treatments

A respiratory outbreak began in February of 2010. Initially, a cow in mid-lactation and a dry cow were found dead on the same day with no prior clinical signs. Gross postmortem examination revealed more than 75% of the lung fields in both cows were consolidated with severe fibrinous bronchopneumonia; fibrin and fluid were present in the thoracic cavity of both cows. A presumptive diagnosis of fibrinous bronchopneumonia was made based on necropsy results. The extensive lung lesions

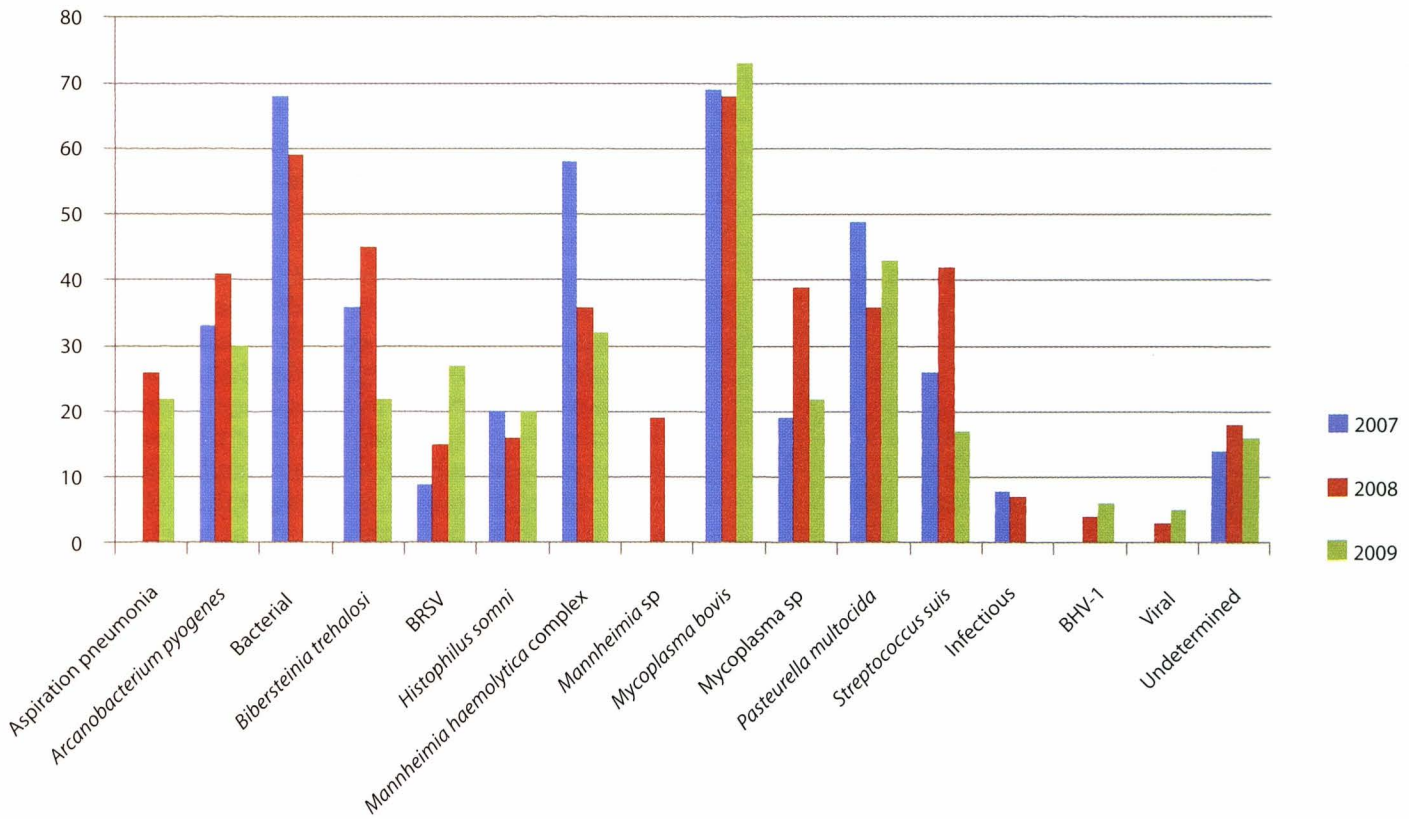

Figure 1. Number of cases of respiratory disease in dairy cattle by diagnosis at the California Animal Health and Food Safety Laboratory System 2007-2009.

suggested the cows may have been sick for several days. The herd veterinarian walked through all pens on the farm looking for signs of pneumonia in other cattle, and observed none. Two days later, the veterinarian was called to necropsy three more cows that died with similar histories. Necropsy findings were similar to the first two cows, and lung tissue samples were submitted to the Wisconsin Veterinary Diagnostic Laboratory for bacteriology and virology.

At that time, the herd veterinarian contacted two of the authors (VSC, DAB) regarding the case. Although the remaining cows appeared normal, the entire herd was vaccinated with intranasal infectious bovine rhinotracheitis/parainfluenza-3 (IBR/PI_3) vaccine[c] in case a virus was involved. The day following herd vaccination, two more cattle were found dead, and postmortem findings were similar to the previous cases. Due to the peracute course of disease and because the owner and veterinarian had not observed any antemortem clinical signs of respiratory disease, any cow showing depressed milk production while in the milking parlor was immediately treated with a systemic antibiotic[d] labeled for treatment of bovine respiratory disease (BRD). Within one week of the initial case, 10% of the herd had received systemic antibiotic therapy.

Based on clinical signs and a history consistent with other cases, a tentative diagnosis of acute *B. trehalosi* pneumonia was made, and it was recommended that the entire herd be vaccinated with a *M. haemolytica* bacterin/toxoid.[e] This recommendation was based on three factors: first, the pneumonia could possibly be caused by *M. haemolytica*; second, there are antigenic similarities between *M. haemolytica* and *B. trehalosi*;[1,13] and finally, two of the authors (VSC, DAB) had used the vaccine in previous cases with favorable results. Since that time, at least one study has shown a decrease in severity of pneumonia caused by *B. trehalosi* when a *M. haemolytica* bacterin/toxoid was used in a challenge model (Pfizer Animal Health, Study report 33828lls, Kalamazoo, MI).

During the next seven days, five more cows died in spite of antibiotic treatment when milk weight decreased. No additional cases occurred after that time. None of the cows identified as sick during the outbreak responded to any antibiotic, and cows that died were in mid- to late-lactation.

Pneumonia was not diagnosed in cows with less than 20 days-in-milk, and the outbreak did not spread to dry cow pens or to heifer groups considered at risk through direct contact. In total, 12 cows died with very similar gross necropsy findings, and an additional 10 cows were eventually culled due to low milk production. All culled cows had been treated with antibiotics based on decreased milk production, rather than clinical signs of BRD.

No viruses were isolated from lung samples from multiple cows. *B. trehalosi* was isolated in numerous colonies from a moderate growth of mixed flora (*B. trehalosi* and *P. multocida*). The antimicrobial sensitivity pattern, utilizing the Trek Sensitivity Titer panel,[f] demonstrated susceptibility to most antimicrobials; however, treatment responses were very poor.

Case 2

History

A total of 189 beef bulls and steers weighing approximately 500 lb (227 kg) were purchased at auction markets for a backgrounding facility during the summer of 2011. The cattle were assembled over several days. Approximately one month after the first cattle arrived, 181 additional cattle of similar type and origin were purchased and co-mingled with the original group. During the previous several years, the death loss at this facility was 1-3% when receiving similar cattle.

Cattle were processed the morning after arrival at the backgrounding facility. Vaccinations included a modified-live (ML) intranasal IBR-PI_3-bovine respiratory syncytial virus vaccine[g] (BRSV); a ML IBR-bovine viral diarrhea virus (types 1 and 2)-PI_3-BRSV vaccine[h] administered subcutaneously; a 7-way clostridial bacterin-toxoid/*Histopholis somni* bacterin combination;[i] and a combination autogenous *P. multocida-Mycoplasma bovis-M. haemolytica* bacterin.[j] In addition, all cattle were treated metaphylactically with ceftiofur.[d] Two weeks later, all calves were revaccinated with ML IBR, BVDV, PI_3, BRSV vaccine;[h] 7-way clostridial bacterin-toxoid/*H. somni* bacterin combination;[i] and autogenous *P. multocida-M. bovis-M. haemolytica* bacterin.[j] Rectal temperatures were taken, and animals with a rectal temperature greater than 104.5° F (40.3° C) were administered tulathromycin[k] and flunixin meglumine.[l]

Cattle were fed a soyhull-based commodity mix twice daily at 5 lb (2.3 kg)/hd/day to supplement grass. Cattle were observed during feeding to identify sick cattle. Animals that were depressed or refused to eat were presumed to have BRD, and were moved to the hospital where the rectal temperature was taken. If febrile, they were treated with tulathromycin[k] at label dose.

Clinical findings and treatment outcomes

Cattle were first diagnosed with respiratory disease approximately 30 days after the second group of cattle arrived. Deaths due to acute pneumonia occurred over the next 40 days. This was the first time in the backgrounding yard's history that calves died without being identified as sick. Cattle responded very poorly to treatment.

At necropsy, severe lung consolidation was observed, with over 75% of the lung field involved in most

cases. Fibrin and fluid were present in the pleural cavity of several cases. No viruses were isolated from laboratory submissions at the University of Kentucky Veterinary Diagnostic Laboratory. Bovine viral diarrhea virus was found with polymerase chain reaction (PCR) testing of lung tissue from a calf that died late in the outbreak. Heavy growth of *B. trehalosi* was commonly cultured, and several calves had a mixed (*M. bovis* and *B. trehalosi*) infection. In total, 37 calves died, equating to a 10% death loss. Ten calves were necropsied, and samples were submitted from eight calves with similar laboratory results. Cattle examined at the diagnostic laboratory were equally represented from both purchase groups.

Case 3

History

A 200-cow dairy experienced a BRD outbreak in eight-week-old Holstein heifers. Calves on this farm were not routinely vaccinated with respiratory vaccines early in life. Three heifers were treated for respiratory disease with several different antibiotics during a two-week period, including tulathromycin,[k] ceftiofur hydrochloride,[m] florfenicol,[n] and enrofloxacin;[o] flunixin meglumine[l] was administered as adjunct therapy. The calves were nonresponsive to treatment, and all three calves died of clinical pneumonia. A necropsy was performed on a fourth heifer that died later after showing similar clinical signs. Several more calves with a similar course of disease were necropsied following death of the fourth animal.

Necropsy findings

At necropsy, 50% of each lung was congested; no other lesions were observed. No pleural adhesions or abscesses were present. A lung sample was submitted to the Murray State University Breathitt Veterinary Center for bacterial culture and susceptibility testing, and a pure culture of *B. trehalosi* was identified. No viruses were identified using PCR or virus isolation.

The farm owner instituted a vaccination program using *M. haemolytica* bacterin-toxoid[e] at six weeks of age. No deaths due to pneumonia have occurred since the vaccination program was initiated.

Discussion

In the United Kingdom, *B. trehalosi* was reported to cause severe fibrinous bronchopneumonia with pleuritis in both calves and cows.[11] Septicemia in cattle has also been documented.[15] In these cases, the organism has been isolated both in pure culture and in mixed growth.[6,11,15] It is now considered part of the BRD complex in the United Kingdom and Europe.[6]

In contrast, little has been reported about this bacterial pathogen in North America. Recent outbreaks of pneumonia in wild, bighorn sheep in Colorado have been attributed to both *M. hemolytica* and *B. trehalosi*; cattle were theorized to be the source of the pathogens.[16]

The three outbreaks reported here are typical of many that two of the authors (VSC, DAB) have investigated. In adult cattle, the disease often begins in production phases not associated with high stress, such as mid- to late-lactation dairy cattle and pregnant beef cattle on pasture, with death occurring within 12-36 hours after the first clinical signs are observed. The death rate is high in spite of aggressive antimicrobial and supportive therapy. In all cases, gross necropsy lesions included severe pneumonia occupying over 50% of the lung field. Often, severe fibrinous attachments and fluid in the thoracic cavity (Images 1 and 2) are present. Necropsy examination cannot differentiate acute pneumonia caused by *B. trehalosi* from that caused by *M. haemolytica*. In the majority of cases, virus isolation and PCR have not revealed a co-infection with common viruses. Pure *B. trehalosi* cultures, as well as mixed infections with other common respiratory bacterial pathogens, have been seen. The BRD outbreaks often continue until 10 to 15% of the herd has been clinically affected, and infected animals often die of the infection. Cross protection has been observed when cattle are vaccinated with a *M. haemolytica* bacterin-toxoid containing high levels of leukotoxoid and cell wall antigen.[e]

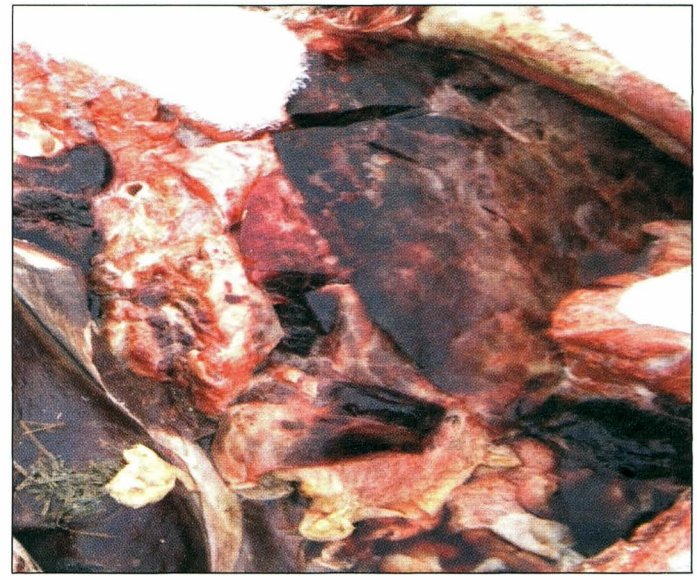

Image 1. Severe consolidation and fibrin in the lungs of an adult Holstein cow, dead within 24 hours of first clinical signs. The dark hemorrhagic lung is indicative of an acute pneumonic lesion.

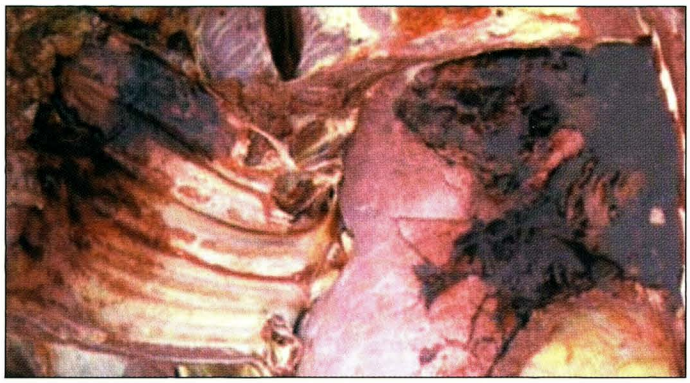

Image 2. Lungs from a 600 lb beef-cross steer with *Bibersteinia trehalosi* pneumonia. Note the dark hemorrhagic areas with consolidation.

Conclusions

Practicing veterinarians and laboratories should monitor for *B. trehalosi* to determine if it is an emerging bacterial pathogen in the BRD complex in North American cattle. It is important for veterinary diagnostic laboratories to further differentiate presumed *M. haemolytica* isolates from *B. trehalosi*.

Endnotes

[a]OmniGen-AF®, Phibro Animal Health, Ridgefield Park, NJ
[b]MTB-100®, Alltech Biotechnology, Alabang, Muntinlupa City 1781 Philippines
[c]TSV-2®, Pfizer Animal Health, New York, NY
[d]Excede™, Pfizer Animal Health, New York, NY
[e]One Shot®, Pfizer Animal Health, New York, NY
[f]Trek Diagnostic Systems, Inc. Cleveland, OH
[g]Inforce™ 3, Pfizer Animal Health, New York, NY
[h]Bovi-Shield GOLD® 5, Pfizer Animal Health, New York, NY
[i]Vision® 7/Somnus, Merck Animal Health, Summit, NJ
[j]Autogenous Pasteurella/Mycoplasma/Mannheimia, Newport Laboratories, Worthington, MN
[k]Draxxin®, Pfizer Animal Health, New York, NY
[l]Flunixin, Norbrook Laboratories, Newry, BT35 6JP, CO Down, Northern Ireland
[m]Excenel®, Pfizer Animal Health, New York, NY
[n]Nuflor®, Merck Animal Health, Summit, NJ
[o]Baytril®, Bayer Healthcare, Animal Health Division, Shawnee Mission, KS

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PREVENT *SALMONELLA* BEFORE IT STEALS YOUR PROFITS.

By Dr. Gary Neubauer, Senior Manager, Pfizer Animal Health Cattle Technical Services

Decreased milk production, higher cell counts and chronic weight loss are strong indications that something is wrong with cows in your herd and immediate action is needed. But how often do you consider *Salmonella* as the cause? The truth is, not often enough.

While the clinical signs of *Salmonella* are easy to identify — explosive diarrhea, dramatic production decrease, weakness, fever, dehydration — dairy cattle often do not display these signs, and the disease can go unnoticed for weeks or even months. Subclinical *Salmonella* can reduce herd performance[1] and, even worse, it can spread from animal to animal, infecting the entire herd in a short amount of time.

Subclinical salmonellosis can develop as a result of exposure to pathogen carriers of the disease. These carriers can exist as active carriers that shed the *Salmonella* organism in manure and/or milk, as symptom-free carriers that infrequently shed organisms or as dormant carriers that harbor *Salmonella* but do not shed bacteria at the time.

Making management more challenging, cattle can move among these carrier states. These carriers can infect the rest of the herd through fecal-oral contamination of bacteria shed during periods of stress such as pen moves or calving.

Help prevent *Salmonella* in your herd by partnering with your veterinarian on a *Salmonella* control program for your operation. Discuss the role that vaccination can play in that plan. Key elements to a *Salmonella* control program include strict sanitation protocols, helping prevent the spread of the bacteria, and good maternity and newborn management.

Reducing your risk of *Salmonella* is important to protect your herd and bottom line. Don't wait until you've seen a clinical outbreak and it's too late. Start working on a program today. To learn more, visit www.SalmonellaRisk.com for information about *Salmonella* prevention and control on your operation.

[1] Hermesch DR, Thomson DU, Loneragan GH, Renter DR, White BJ. Effects of a commercially available vaccine against *Salmonella* enterica serotype *Newport* on milk production, somatic cell count, and shedding of *Salmonella* organisms in female dairy cattle with no clinical signs of salmonellosis. *AJVR* 2008;69(9):1229-1234.