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Citation	Hales, K.E.. 2024. Review: Summary of the Special Issue on liver abscesses in cattle and thoughts on future research*. <i>Applied Animal Science</i> , 40(3). https://doi.org/10.15232/aas.2024-02553
Citable Link	https://hdl.handle.net/2346/98565
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HEALTH, NUTRITION, PHYSIOLOGY, AND PRODUCTION AND MANAGEMENT: *Review* *Conclusions and research recommendations going forward*

REVIEW: Summary of the Special Issue on liver abscesses in cattle and thoughts on future research*

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ABSTRACT

Objective: My objective was to summarize 16 original research manuscripts and 1 perspectives and commentary contribution that were submitted, peer reviewed, and accepted in this Special Issue on liver abscesses in cattle.

Materials and Methods: A summary of key points made in the Special Issue articles is provided. Additional conclusions and thoughts about future directions of research to address liver abscesses (LA) in cattle are offered.

Results and Discussion: This Special Issue represents the current understanding of the etiology, blood chemistry biomarkers, dietary and management strategies, and mitigation strategies for LA in cattle used in the feedlot industry throughout the United States and Canada. Seventeen articles from researchers and industry professionals studying LA in cattle are included, with studies ranging from practical dietary intervention strategies to experiments designed to understand the mode of action and the etiology of LA development.

Implications and Applications: Liver abscess disease is a multifactorial, polymicrobial disease that affects multiple organ systems within the body, reflecting complex interactions among the host, environment, and pathogens. The pathogenesis of this disease needs to be further examined, and basic and applied research approaches should be employed to advance our understanding of liver abscesses in cattle.

Key words: cattle, liver abscesses, *Fusobacterium necrophorum*, special issue

The author has not declared any conflicts of interest.

*The American Registry of Professional Animal Scientists gratefully acknowledges the financial contributions of sponsors to pay the open access publication fees for all articles in this Special Issue, “Liver Abscesses in Cattle.” The sponsors are listed in the Acknowledgments section.

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INTRODUCTION

Liver abscesses (LA) affect 0% to 95.5% of feedlot cattle on an individual-pen basis (Grimes et al., 2024) and, in severe cases, can decrease feed intake, ADG, G:F, and hot carcass weight (HCW; Brink et al., 1990). The cost of LA, which are responsible for 70% of all liver condemnations in the United States (Brown and Lawrence, 2010), is greater than \$400 million annually because of condemned livers, increased carcass trimming, and diminished offal and carcass values (Herrick et al., 2022). This financial burden to the cattle feeder and beef processor represents a decrease in the efficiency and sustainability of beef production.

KEY POINTS BY TOPIC

New Perspectives on a Historic Fed-Cattle Issue Were Reported by Broadway et al. (2024)

- Liver abscesses are a multifactorial, polymicrobial disease with effects on productivity and profitability in all stages of the beef production continuum.
- Lack of viable methods to detect LA before slaughter complicates research designed to evaluate mitigation strategies and disease etiology.
- Understanding the timing of LA development and whether an abscess can resolve is challenging because LA are difficult to reliably detect in live cattle.
- *Fusobacterium necrophorum* subspecies *necrophorum* have been implicated as the primary causative pathogens. Nonetheless, recent data suggest that *Salmonella* also could be involved in development and severity of LA.
- Because model studies have failed to induce LA when a diet likely to cause ruminal acidosis was fed in absence of an intraruminal inoculation of *F. necrophorum* subspecies *necrophorum*, it is unclear whether ruminal acidosis and rumenitis are required in the development of LA.

Detection and Quantification of the Microbes *Fusobacterium necrophorum* and *Fusobacterium varium*

- An assay was developed to detect and quantify *F. necrophorum* and *F. varium* in ruminal contents of cattle (Deters et al., 2024a).
 - *Fusobacterium necrophorum* subspecies *necrophorum* was quantified in ruminal contents of 22% of cattle without LA and 29% of cattle with LA.
 - Subspecies *funduliforme* and *varium* were present in 98% and 100% of ruminal content samples, respectively. These subspecies and mean concentrations of subspecies did not differ between cattle with and without LA.
 - A small percentage of ruminal contents harbored the subspecies *necrophorum*, suggesting that it is not normally part of the ruminal microbial community. Nonetheless, subspecies *funduliforme* and *varium* were highly prevalent in all ruminal content samples evaluated.
 - Although *F. varium* is a pathogen, it is not known whether it contributes to the development of LA.
- The first report of isolation of *F. varium* from LA and ruminal and colonic epithelial tissues of cattle was reported by Deters et al. (2024b).
 - *Fusobacterium varium* was isolated from
 - 10% of LA,
 - 77% of ruminal epithelial tissues,
 - 45% of colonic epithelial tissues,
 - 87% of ruminal contents, and
 - 70% of colonic contents.
 - Prevalence in ruminal and colonic tissue suggests *F. varium* can invade tissue and potentially cause rumenitis, but because it was isolated from LA with low frequency, it is not likely involved in the development of LA.
 - Additional research is necessary to evaluate *F. varium* and whether it can cause rumenitis or LA in cattle.

Dietary Strategies to Mitigate LA Prevalence

- Standard finishing cattle diets with or without tylosin phosphate using an industry standard roughage concentration versus titrated roughage concentrations in diets without tylosin phosphate was reported by Word et al. (2024).
 - Increasing roughage (corn stalks) concentration increased DMI and decreased final BW, ADG, and G:F.
 - Hot carcass weight did not differ between diets with and without tylosin phosphate when corn stalks were included in the diet at the same concentration; however, HCW decreased linearly as

corn stalk inclusion increased from 7% to 19% of dietary DM.

- Increased corn stalk concentration in the diet led to increased DMI but decreased NE_g and HCW in cattle fed the same number of days.
- Prevalence of LA decreased linearly with increased corn stalk inclusion, but increasing corn stalk inclusion did not affect the prevalence of A+ abscesses adhered to the diaphragm.
- Inclusion of tylosin phosphate decreased A+ abscesses adhered to the diaphragm.
- Increasing roughage NDF concentration and bulk density of steam-flaked corn was reported by McDaniel et al. (2024a).
 - Dry matter intake increased linearly as roughage NDF increased, but no differences in ADG or G:F were observed.
 - Marbling score responded quadratically to roughage NDF concentration, being greater for steers fed 3% versus 4.5% or 6% roughage NDF.
 - Total percentage of LA decreased linearly as roughage NDF increased from 3% to 6% of DM as did the presence of A+ abscesses.
 - Total LA were 13.9 percentage points less for steers fed 412 versus 309 g/L (32 vs. 24 lb/bu or 33% vs. 69% starch availability) steam-flaked corn.
 - Increasing roughage NDF concentration and bulk density of steam-flaked corn are dietary strategies that can decrease LA prevalence at slaughter.
- Different strategies for forage inclusion to control LA were reported by Paterson et al. (2024).
 - Four dietary treatments were used: (1) a 7.5% forage (barley silage) diet (DM basis) with 11 mg/kg tylosin phosphate; (2) a diet without tylosin phosphate; (3) a diet in which forage concentration was decreased every 42 d to static concentrations for the final 84 d (forage represented 15%, 9%, 3%, and 3% of dietary DM) without tylosin phosphate; and (4) a diet in which forage concentration increased every 42 d to a static concentration for the final 84 d without tylosin phosphate.
 - Steers fed a diet with 7.5% forage (barley silage on a DM basis) with tylosin phosphate had increased ADG versus steers in which forage concentration increased every 42 d and was static the final 84 d on feed.
 - Including a greater concentration of forage early in the finishing period with concentrations decreasing thereafter produced results not different from including tylosin phosphate, with little effect on ruminal fermentation and ruminal microbiota.
 - The proportion of steers with minor LA was less in the diet with 7.5% forage (on a dietary DM

- basis) plus tylosin phosphate and when forage concentration decreased every 42 d to static for the final 84 d on feed (without tylosin phosphate) than in the diets with increasing or decreasing forage concentration every 42 d to static the last 84 d without the inclusion of tylosin phosphate.
- Greater dietary concentrations of forage early in the feeding period, decreasing thereafter, could decrease the proportion of small LA to a level not different from feeding tylosin phosphate without affecting growth performance or carcass characteristics.
 - Timing of forage inclusion could be more detrimental to growth performance and carcass characteristics than minor LA.

Supplementation Strategies to Mitigate LA Prevalence

- Use of calcium magnesium carbonate and tylosin phosphate supplementation on rumination behavior, growth performance, LA prevalence, and carcass characteristics in yearling beef steers was reported by Grimes Francis et al. (2024).
 - Calcium magnesium carbonate decreased DMI by 4.9% but increased time spent ruminating, whereas tylosin phosphate increased DMI by 1.6% and decreased time spent ruminating.
 - Hot carcass weight tended to be less for control than when calcium magnesium carbonate was fed.
 - Feeding tylosin phosphate tended to decrease the percentage of LA by 9.8 percentage points.
 - Although calcium magnesium carbonate altered rumination time, no advantages in growth, carcass characteristics, or LA prevalence were observed.
- Effects of *Bacillus licheniformis* as an alternative for tylosin phosphate to control LA in crossbred finishing beef steers was studied by Hoffinan et al. (2024).
 - No differences in ADG, DMI, or G:F were observed when steers were fed a control supplement (no antibiotic or probiotic), tylosin phosphate the entire feeding period, tylosin phosphate removed the last 65 d on feed, or a supplement containing *B. licheniformis*.
 - Liver abscess prevalence and severity did not differ among treatments.
 - *B. licheniformis* did not exhibit beneficial effects as a strategy to decrease LA prevalence in finishing beef steers.
- Supplementation of *Saccharomyces cerevisiae* CNCM I-1077 and calcium clinoptilolite zeolite were compared with tylosin phosphate and a negative control in dairy-beef crossbred heifers by Theurer et al. (2024).
 - Heifers fed tylosin phosphate had decreased DMI, increased G:F, and decreased cost of gain compared with heifers fed the other treatments.
 - Carcass characteristics did not differ among treatments.
 - Heifers fed *S. cerevisiae* CNCM I-1077 and calcium clinoptilolite zeolite tended to have 6.44 percentage point fewer LA than heifers fed tylosin phosphate, whereas heifers fed the negative control treatment were intermediate.
 - *Saccharomyces cerevisiae* CNCM I-1077 in combination with calcium clinoptilolite zeolite could be a promising mitigation strategy for LA but may decrease growth performance compared with tylosin phosphate.
- Effects of feeding virginiamycin on ruminal acidosis and liver health in growing and finishing beef steers was reported by Rivera et al. (2024).
 - Steers were fed 0 versus 40 mg of virginiamycin daily for the first 50 d, first 100 d, final 50 d, final 100 d, or entire 150 d of the feeding period.
 - Steers fed virginiamycin the first 100 d had greater mean ruminal pH from d 50 to 100 than steers not fed virginiamycin.
 - Steers fed virginiamycin for 150 d had less time with ruminal pH of 5.8 or less than steers fed virginiamycin for the first 50 d or the last 50 d on feed.
 - At slaughter, 3.4% of steers had a LA and 24.3% had lung lesions.
 - Plasma metabolite data were not useful in predicting the presence of LA.
 - Feeding virginiamycin increased plasma alkaline phosphatase and albumin:globulin but was not effective at decreasing LA.
- Effects of dietary composition and feeding management regimen on LA prevalence were reported by Schneid et al. (2024).
 - Steers were fed diets based on steam-flaked corn with 49% or 64% total starch concentrations on a dietary DM basis and fed for consistent feed delivery or randomized variations in feed quantity and feed delivery time.
 - Steers fed the 64% total starch diet had 21.7 percentage points greater LA and 12.7 percentage points greater liver scar prevalence than steers fed a diet with 49% total starch (DM basis).
 - Steers fed the diet with a greater starch concentration had decreased final BW, ADG, DMI, G:F, HCW, marbling score, and calculated YG compared with those fed the lower starch diet.
 - Consistent or inconsistent feed delivery did not affect LA prevalence, growth performance, or carcass characteristics.

LA Associated with Carcass Characteristics and Value

- Historical data gathered by the West Texas A&M University Beef Carcass Research Center and cataloged in 2 databases were reported by Grimes et al. (2024).
 - Abscess prevalence rates differed by liver score across the 2 databases.
 - A- = 7.2% to 7.3%
 - A = 2.7% to 5.3%
 - A+ = 2.3% to 4.8%
 - A+ adhered to diaphragm = 3.7% to 6.2%
 - A+ open abscess = 1.4% to 1.7%
 - A+ adhered and A+ open = 0.8% to 1.3%
 - Carcasses that had severe LA had a HCW that was decreased by 8 to 21 kg compared with carcasses with edible livers.
 - Abscesses were associated with decreased LM area, and A-, A, A+, and A+ adhered abscesses were associated with decreased rib-fat thickness.
 - Percentage of carcasses railed off-line increased with increasing LA severity, particularly for livers with adhered (4.2%), open (9.7%), or adhered and open abscesses (11.9%).
 - Based on evaluation across the years included in the database, LA prevalence is increasing.
 - The prevalence of LA in beef × dairy crossbreds was greater than in purebred Holstein cattle in the 2 databases.
- Carcass information from 2,143 Holstein cattle fed in Texas and Kansas in 2016 and 2017 were reported by Herrick et al. (2024).
 - Carcasses with adhered and open abscesses were associated with decreased HCW (25 kg or 6.6%) versus carcasses with no LA present.
 - Abscesses were associated with increased carcass trim in carcasses with adhered (0.72 kg), open (3.92 kg), or adhered and open (3.39 kg) abscesses.
 - Gross carcass revenue was 5% to 6.4% less in carcasses with adhered, open, or adhered and open LA.
 - Gross carcass revenue decreased when adhered (-\$97.69/carcass), open or adhered (-\$93.86/carcass), and open (-\$121.22/carcass) LA were present.

Blood-Based Biomarkers for Detection of LA

- Blood was collected from beef × dairy crossbred heifers to determine complete blood counts and liver function by Wilson et al. (2024).
 - Heifers with LA had decreased lymphocytes and white blood cell concentrations but an elevated platelet-to-lymphocyte ratio.

- Serum chemistry measures were not affected by presence or severity of LA.
- Although white blood cell concentration was accurate (65.9%) at predicting LA presence, it had poor specificity (54.8%).
- There was a minimal response in complete blood count measurements associated with LA.

Models to Induce LA in Steers

- A study to validate a model to induce LA in steers and assess the contribution of *Fusobacterium* and *Salmonella* on LA formation and severity was reported by McDaniel et al. (2024b).
 - Steers fed a high-forage diet and not infused with *F. necrophorum* had 0% LA, whereas steers fed a diet likely to cause ruminal acidosis, based on steam-flaked corn, and infused with either *F. necrophorum* subspecies *necrophorum* or *F. necrophorum* subspecies *necrophorum* and *Salmonella* had 40% and 50% LA, respectively.
 - Ruminal tissue damage was more severe when steers were infused with only *F. necrophorum* subspecies *necrophorum* than with *F. necrophorum* subspecies *necrophorum* and *Salmonella*.
 - Feeding a diet that was likely to cause ruminal acidosis without an intraruminal bacterial inoculation caused mild ruminal acidosis but not LA.
 - Feeding an acidotic diet with intraruminal bacterial inoculation is a viable model to induce LA.
- Ileal tissues were collected from steers with and without experimentally induced LA to study genetic expression (Lindholm-Perry et al., 2024).
 - Twenty-six genes were differentially expressed in steers with LA versus those without LA.
 - Two of the 26 genes are components of the cytochrome c oxidase enzyme in the electron chain transport pathway, both of which were downregulated in steers with LA.
 - Other genes identified are responsible for transport of compounds across cell membranes, protection of RNA, and protein products.
 - The ileum is likely associated in some way with LA development because ileal tissue undergoes cellular changes in steers with LA.
- Injecting *F. necrophorum* subspecies *necrophorum* into the peripheral circulation or hepatic portal vein of preruminant Holstein calves failed to induce LA as reported by Cox et al. (2024).
 - Giving calves an intrajugular infusion of sterile saline or *F. necrophorum* ssp. *necrophorum* at 1×10^7 , 1×10^9 , or 1×10^{11} failed to result in LA.
 - Whole-blood monocyte count was greater in calves that received the greatest dose of *F. necrophorum* (1×10^{11}) 3 and 5 d after the challenge, and the neutrophil-to-lymphocyte

- ratio was greater 7 d after the challenge in calves that received *F. necrophorum* (1×10^{11}).
- In a separate subset of calves, an intraportal infusion of sterile saline or *F. necrophorum* ssp. *necrophorum* at 1×10^6 , 1×10^8 , and 1×10^{10} did not induce LA.
 - Intraportal inoculation increased monocyte and neutrophil counts in the group that received the intermediate concentration of *F. necrophorum* (1×10^8).

Conclusions and Research Recommendations Going Forward

The articles within the Special Issue represent the current scientific understanding of LA in cattle. These articles encompass etiology, blood biomarkers, mitigation and management strategies, effects on carcass value, tissue transcriptome profiles, methods for detection of different subspecies of *F. necrophorum*, and viable and unsuccessful models to induce LA.

Severe LA, specifically A+, A+ adhered, A+ open, and A+ adhered and open abscesses, appreciably decrease HCW and s.c. fat stores, while increasing carcass trimming (Grimes et al., 2024). Percentage and severity of LA can be controlled by feeding tylosin phosphate (Word et al., 2024), increasing concentrations of roughage NDF, or including a heavier bulk density of steam-flaked corn in the diet (McDaniel et al., 2024a). Likewise, decreasing the total dietary starch concentration decreases LA prevalence and liver scars (Schneid et al., 2024). The importance of liver scars is not fully understood, but presumably they represent a resolved abscess.

White blood cell concentration is a potential indicator of LA presence, but it has poor specificity (Wilson et al., 2024). Many of these biological indicators could indicate infection, inflammation, or stress (Pagana et al., 2015) not necessarily caused by a LA, which is the likely reason for their poor specificity. From a practical standpoint, if LA could be detected while cattle were on feed, it is unclear how this would change current feedlot management practices. A single small LA could have the potential to resolve and leave only a scar on the liver, but larger A+ abscesses, particularly those abscesses adhered to the diaphragm, are unlikely to resolve. Furthermore, the time necessary for a LA to develop and resolve is not known. Additional research on biomarkers of active LA is necessary to better understand the timeline of abscess development and their potential to resolve.

Recently, *F. varium* was identified as the dominant *Fusobacterium* species within the rumen, which was contrary to the generally accepted belief that *F. necrophorum* was thought to be the dominant ruminal species (Schwarz et al., 2023). Indeed, *F. varium* and *F. necrophorum* have similar colony morphology and both use lactate and lysine. Therefore, it is likely that *F. varium* has been pre-

viously mischaracterized as *F. necrophorum* (Schwarz et al., 2023). *Fusobacterium varium* was isolated from 10% of LA, 77% of ruminal epithelial tissues, 45% of colonic epithelial tissues, 87% of ruminal contents, and 70% of colonic contents (Deters et al., 2024b). The prevalence in ruminal and colonic tissue suggests *F. varium* can invade tissue and potentially cause rumenitis. Perhaps ruminal acid accumulation facilitates tissue invasion by *F. varium*? Nonetheless, because it is isolated from LA with low frequency, it is unlikely to be involved in abscess development (Deters et al., 2024b). Could *F. varium* be the cause of rumenitis observed at necropsy or slaughter and have little involvement in the development of LA? Furthermore, if *F. varium* has the potential to cause rumenitis, is ruminal acidosis necessary for LA formation? Additional research is necessary to evaluate the association of *F. varium* with the development of LA.

It is unclear whether *Salmonella* is involved in the development of LA, but its isolation from LA confirms the polymicrobial nature of the disease. When *Salmonella* was included in the bacterial inoculation used to induce LA in growing steers, the prevalence and severity of LA was increased (R. Broadway, ARS, USDA, Lubbock, TX, personal communication). *Salmonella* typically colonizes the ileum, and the ileum is one entry point of *Salmonella* to the lymphatic system. The confirmation that ileum tissue experienced cellular changes in steers with a LA (Lindholm-Perry et al., 2024) suggests a potential for ileal involvement in the development of LA. Similarly, after *Salmonella* was isolated from an active abscess, Amachawadi and Nagaraja (2015) suggested the small or large intestine may be involved in the development of LA. Research employing culture techniques to isolate *Salmonella* from LA and evaluate hindgut tissue histology and cellular changes will further advance our understanding of the etiology of LA formation.

Based on the research presented in this Special Issue, future LA research should focus on addressing the following themes:

1. Exploring pathogens associated with LA development, specifically *Salmonella* and *F. varium*;
2. Understanding how ruminal acidosis is associated with development of LA;
3. Determining the relationships among rumenitis, *F. varium*, and LA development;
4. Development of effective mitigation or management strategies to prevent LA in finishing cattle;
5. Identifying accurate and specific physiological indicators or biomarkers of LA in live cattle and using biomarkers to determine the timeframe for LA formation and ability to resolve while cattle are on feed;
6. Exploring and elucidating the involvement of the small and large intestine and barrier dysfunction in LA formation;

7. Better understanding the differentially expressed genes in cattle with and without LA to determine the influence of genetics on this disease;
8. Determining how cattle breed types affect LA prevalence; and
9. Identifying how early life calf management affects the prevalence of LA at slaughter.

APPLICATIONS

Liver abscesses are the result of a multifactorial, polymicrobial disease process that affects multiple organ systems within the body because of complex interactions among the host, environment, and pathogens. The pathogenesis of this disease needs to be further explored so that effective mitigation strategies can be developed in which animal productivity is not negatively affected. Basic and applied research approaches should be employed to advance our knowledge of LA in cattle.

ACKNOWLEDGMENTS

The editorial team of *Applied Animal Science* thanks the following corresponding authors for their submissions to this Special Issue: R. Broadway, K. Hales, T. Lawrence, A. Lindholm-Perry, V. Machado, T. Nagaraja, G. Ribeiro, K. Samuelson, Z. Smith, L. Tedeschi, M. Theurer, D. Woerner, and A. Word.

The American Registry of Professional Animal Scientists (ARPAS) gratefully acknowledges the financial contributions of the following sponsors to pay the open access publication fees for all articles in the Special Issue: Agri Research Center, Elanco Animal Health, Kemin Industries, Merck Animal Health, Midwest PMS, Plains Nutrition Council, Phileo Lesaffre, and Texas Tech University Davis College of Agricultural Sciences and Natural Resources. Arm and Hammer was a financial supporter of the ARPAS Symposium on Liver Abscesses in Cattle, July 20, 2023, which was, in part, an impetus to develop this Special Issue. Thank You.

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