

**Epidemiology of Toe Tip Necrosis Syndrome in
Western Canadian Feedlot Cattle**

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ABSTRACT

Lameness continues to cause significant problems in profitability, productivity, and animal welfare in the feedlot industry. Toe tip necrosis syndrome (TTNS) is a new name for a previously reported condition. By definition, TTNS is separation of the apical white line with tissue necrosis and clinical lameness. This definition includes complications such as pedal (P3) osteitis, middle (P2) and proximal (P1) phalangeal osteomyelitis, tendonitis, tenosynovitis, cellulitis, and embolic pneumonia. Anecdotal experiences from practitioners report this lameness in feedlot cattle will develop within weeks after feedlot entry. Often the hindlimbs, specifically the lateral claw, are affected where a separation of the dorsal wall and sole will be noticed. Secondary infections will progress deeper into the foot and become systemic. Unfortunately, despite treatment, these animals can become very lame and will need to be euthanized. The overall objective of this project was to describe the epidemiology of TTNS in western Canadian feedlot cattle. The specific objectives were 1) to use clinical examinations, imaging modalities, and necropsy findings to aid in description, classification, and characterization of TTNS lesions, 2) to describe the epidemiology of TTNS in feedlot cattle, and 3) to evaluate risk factors for TTNS.

Upon further investigation into this arrival related condition it became apparent that there were many different descriptors: P3 necrosis, toe abscess, apicus necrotica, apical pedal bone necrosis or toe necrosis. These names and descriptors of toe tip lesions were based on anecdotal experiences and previous case reports. As a result, traditional epidemiological approaches that included field investigations, clinical and necropsy examinations were implemented to identify, characterize and describe this condition. Based on clinical findings, imaging modalities, and

necropsy specimens examined during September to December 2012, inclusive, a more specific name and descriptive case definition were introduced.

TTNS descriptive epidemiology was described by use of a retrospective database analysis from Feedlot Health Management Services (FHMS) with 702 veterinarian confirmed TTNS cases by necropsy examination. From this database, there were 30% (210/702) of necropsy cases treated for TTNS and 70% of cases (492/702) that were not treated. Of those animals treated, the mean and standard deviation (median) interval from feedlot arrival to first treatment was 18.9 ± 1.7 d (12 d). The mean (standard deviation) days on feed until death from TTNS was the earliest in grass-fed calves (32.4 ± 22.1 d), followed by auction-derived (40.6 ± 40.6 d), ranch direct (44.1 ± 53.1 d), and back-grounded calves (69.0 ± 75.6 d) ($P < 0.001$). Yearlings were on feed for a mean (standard deviation) days of 37.1 ± 32.0 d when compared to calves at 49.5 ± 57.0 d before death ($P < 0.001$). The greatest proportion of deaths occurred from September to November. There were 96.2% (1,832/1,904) of lots without one case of TTNS and 3.8% (72/1,904) of lots had one or more TTNS cases.

A prospective case-control study to identify TTNS risk factors consisted of 148 total necropsy submissions (82 cases, 66 controls) from three feedlot veterinary practices and 16 feedlots during October 2012 to January 2013, inclusive. Confirmation of feet samples by the principal investigator at the Western College of Veterinary Medicine reduced the total to 135 animals: 67 cases and 68 controls. The measure of agreement (kappa) on classification of TTNS cases and controls between the veterinary practice and WCVM was 0.778 ($P < 0.001$). Bacterial culture results revealed that 75% of pure isolates in TTNS cases were attributed to *Escherichia coli*, *Streptococcus* spp., *Trueperella pyogenes*, *Fusobacterium necrophorum*. TTNS cases were 3.8 times more likely than control animals to have BVDV isolated (95% CI 1.7-8.5; $P < 0.001$).

TTNS animals were 2.2 times more likely than control animals to have histopathological evidence of vasculitis (95% CI 1.0-4.6; $P = 0.04$). BVDV samples were 11.2 times more likely to show histopathological evidence of vasculitis than non-BVDV samples (95% CI 4.7-27.0; $P < 0.001$). A decreased difference was found in sole thickness at the toe tip ($P < 0.001$). There was no evidence of pedal bone rotation between case and control animals ($P = 0.15$).

In summary, TTNS is a specific term for apical white line separation with tissue necrosis and clinical lameness. A practitioner's field diagnosis of TTNS based on apical white line separation and tissue necrosis is accurate on clinical signs alone. TTNS is a transport or arrival related condition in feedlot cattle that has a propensity for cases to cluster together. Pure bacterial isolates provide an understanding of the pathogens responsible for TTNS and that environmental pathogens contribute to an ascending infection. BVDV, vasculitis and apical sole thickness were risk factors associated with TTNS; however, their exact role requires further investigation.

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CHAPTER 1: INTRODUCTION AND LITERATURE REVIEW

1.1 INTRODUCTION

By definition, lameness is any abnormality of gait displayed by an animal (Greenough, 2007). There are many different causes of lameness including traumatic, infectious, and nutritional (Radostits *et al*, 2007). Lameness affects animal welfare, productivity and economics in feedlot cattle. Lameness causes pain in affected animals. It is not known how much pain that a lame animal experiences but the change in locomotion and abnormal body positions are indicative of the animal being uncomfortable (Greenough, 2007). Even a layperson who is untrained in animal health and welfare can easily identify a lame, painful animal based on the change in gait. The National Farm Animal Care Council has recognized that feedlot lameness, notably toe tip necrosis, is an animal welfare issue and that further research is needed to understand risk factors, prevalence, and costs to Canadian feedlot operators in the most recent Scientific Report (Schwartzkopf-Genswein *et al.*, 2012). The animal's change in behavior due to pain can reduce the ability to approach a feed source. Kruse *et al* (2013) documented that lame animals have a significant reduction in average daily gain. A University of Nebraska record review of five large western feedlots showed that ~70 percent of non-performing cattle were lame (Griffin *et al*, 1993). In addition, the same study estimated that salvageable lame animals were 53% of their original value. It has been estimated that lameness costs the Alberta feedlot industry \$42.5 million, based on 2.5 million cattle being finished annually (Demmans *et al.*, unpublished). As such, lameness in beef cattle, particularly feedlot cattle, has garnered more interest by the beef industry to understand the overall impact of this condition.

1.2 ANATOMY OF BOVINE DISTAL LIMB

The bovine distal limb consists of four digits; two digits of which are weight bearing and two that are non-weight bearing, the latter are referred to as dewclaws (van Amstel and Shearer,

2006). As depicted in Figure 1.1 each weight bearing digit comprises three phalangeal bones termed: proximal (P1), middle (P2), and distal (P3). The distal phalange is completely encased within the claw capsule. The navicular bone is a distal sesamoid bone and is located palmar/plantar to the middle phalange. The joint space between the distal and middle phalanges is called the distal interphalangeal joint. The joint between the middle and proximal phalange is termed the proximal interphalangeal joint. The metatarsophalangeal joint connects the metatarsal and proximal phalange.

Three extensor tendons are located on the dorsal aspect of the limb and transverse distally (Dyce *et al*, 2002). The common digital extensor tendon bifurcates and inserts on the extensor processes of the distal phalanges. The deep digital flexor (DDF) tendon is attached to the palmer/plantar aspect of the distal phalange. The DDF follows the superficial digital flexor tendon, which is attached to the middle of the proximal phalange, as the tendons ascend proximally. Tendon sheaths encase these tendons and contain synovial fluid as lubrication for ease of movement.

The corium is a vascularized dermal structure that supports the horn-producing epidermis (van Amstel and Shearer, 2001). They are four regions of corium: perioplic, coronary, laminar, and solar. Perioplic corium is located below the skin-horn junction and extends to cover the heel bulb. The coronary corium is found between the perioplic corium and laminar corium. The laminar corium is parallel to the distal aspect of the pedal bone. The solar corium covers the ventral portion of the foot between the laminar and perioplic corium. These regions of the corium produce different types of keratinocytes and subsequently varying strengths of horn.

The distal phalange or pedal bone is suspended in the claw capsule by interdigitation of dermal and epidermal laminae (van Amstel and Shearer, 2006). This interdigitation is between

the inner aspect of the claw capsule and the corium that covers the dorsal aspect of the pedal bone (Greenough, 2007). The ventral aspect of the pedal bone is concave, and as a result, there are two points that with enough pressure on the solar corium can predispose to toe or sole ulcers (van Amstel and Shearer, 2006).

The claw consists of keratinocytes and forms a capsule around the corium and functions as a shock absorber for the distal limb. It includes the wall and sole. The wall can be further divided into abaxial (outside) and axial (inside). The sole is the bottom of the claw that merges to the heel-sole junction and connects to the wall. The white line unites the wall and sole. Horn of the white line is produced from epidermis that originates from the laminar corium (van Amstel and Shearer, 2001). White line horn is the softest horn of the claw and corresponds to a weak point that can be vulnerable to damage. In the equine species, Budras *et al* (1998) mention the horn tubules in the white line are very short and are a potential entrance for ascending bacterial pathogens to reach the corium.

Horn of the dorsal wall grows at a rate of 5 mm a month (Greenough, 1997; Dyce *et al*, 2002). Horn of the sole grows at 3 mm a month (Greenough, 1997). The toe angle in a standing animal is approximately 50 degrees (Dyce *et al*, 2002). Greenough (2007) reported the apical sole thickness of a normal mature cow to be 5-7 mm, and the sole ventral to the pedal bone to be 15 mm.

1.2.1 WEIGHT DISTRIBUTION OF DISTAL LIMB

The front feet bear more weight than the rear feet due to forelimb musculature and the animal's center of gravity (van Amstel and Shearer, 2006). It has been reported by Greenough (2001) that 60% of animal's body weight is borne on the forelimbs and 40% is supported on the hindlimbs. In the front foot, the medial claws bear more weight than the lateral claw in comparison to the rear foot where more weight is borne on the lateral than the medial claw (van

Amstel and Shearer, 2006). Medial and lateral claws of the hind foot have anatomical differences. The lateral claw is larger and has a greater surface area for weight bearing than the medial claw (Greenough, 2001; van Amstel and Shearer, 2006). When the animal places the hind foot down during walking the weight-bearing initially occurs on the lateral claw (van Amstel and Shearer, 2006). The major weight bearing structures within the claw are the distal abaxial wall and heel bulb, and less commonly, the sole (Mills *et al*, 1988).

1.2.2 VASCULATURE OF DISTAL LIMB

Arterial blood supply in the hindlimb is supplied by the dorsal common digital artery (Vermunt and Leach, 1992). As shown in Figure 1.2 this artery branches into the proper digital artery leading into the medial and lateral claws; in addition, arterial branches will enter the heel bulb. The proper digital artery will enter the axial foramen in the pedal bone. As the proper digital artery travels through the pedal bone it forms a terminal arch. This arch forms a “hair-pin” loop that includes microcirculation of arcuate arteries and arteriovenous anastomoses. The arteriovenous anastomoses are shunts between the arteriole and venule in the capillary bed which aids in the passive movement of blood (Greenough, 2007). The vasculature will travel from the apex of the toe, and then course axially and abaxially towards the sole.

The venous circulation reflects the arterial system and consists of anastomosing vessels that form into the dorsal proper digital vein and common dorsal digital vein (Vermunt and Leach, 1992). There are venous valves in the distal limb that aid in blood circulation (Greenough, 2007).

1.3 CANADIAN BEEF PRODUCTION

Canadian beef production occurs in multiple stages. These production stages include cow-calf, background-finishing, feedlot, and slaughter. Canadian beef production is concentrated in western Canada (British Columbia, Alberta, Saskatchewan, Manitoba) and as of January 1, 2012 these provinces represented 86% (3.65/4.23 million beef cows) of the country’s beef cows

(Canadian Beef, 2014). The provinces of Alberta and Saskatchewan feed ~70% of Canada's finished beef (CanFax, 2014). Economically, beef production in the year 2011 generated \$25.96 billion to the Canadian economy, which increased 5.5% from the previous year (Statistics Canada, 2011). Beef production in western Canada is cyclical as demonstrated in Figure 1.3. While this thesis focuses on lameness in the feedlot animal, an understanding of Canadian beef production is required; further background information about Canada's beef production can be found in Appendix A.

1.4 LAMENESS IN FEEDLOT CATTLE

Lameness in feedlot cattle is an economic, production-limiting, and welfare concern. Economically, the return is reduced for lame feedlot animals as productivity declines and treatment costs increase (Cha *et al.*, 2010). In feedlot cattle, lameness has been shown to decrease the average daily gain and increase the total days on feed (Tibbetts *et al.*, 2006). Furthermore lameness negatively impacts the welfare of the animal (Webster, 1986).

Lameness is a clinical sign exhibited by an animal, but is not a diagnosis. Even though lameness is very common in beef cattle there is very little published literature when compared to dairy cattle (Anderson and Rogers, 2001). There are significant losses due to lameness (Griffin *et al.*, 1993). These losses include treatment costs, labour costs, reduced average daily gain, salvage and death losses. Lameness can broadly be classified in the categories of infectious, non-infectious, injury and nutritional causes (Radostits *et al.*, 2007). It has been estimated by Desrochers *et al.* (2001) that 80-90% of lameness will occur distal to the fetlock; however, Griffin *et al.* (1993) report in feedlot cattle that diseases of the feet will account for 70% of all lameness. The most common causes of lameness in feedlot cattle are interdigital necrobacillosis, injuries, and toe abscesses (Miskimins, 2002). Many feedlot lameness conditions arise from etiological pathogens present in the environment (Radostits *et al.*, 2007).

In most circumstances, early diagnosis is important for a successful recovery from lameness. Unfortunately treatment facilities in a feedlot setting are not ideal to examine the feet of cattle as handling chutes have limited access to the animal. In addition, the animal's temperament can make examination a challenge. Since many lameness conditions have similar clinical signs it is not uncommon for these conditions to be misdiagnosed or misclassified (Kruse *et al.*, 2013).

1.4.1 TOE TIP LESIONS IN CATTLE

Practitioners have used many different names to describe toe tip lesions in cattle: P3 necrosis, toe abscesses, apicus necrotica, apical pedal bone necrosis or toe necrosis. The lack of case definitions and different names allows for toe tip conditions to be easily confused and misdiagnosed. Kofler (1999) mentioned that toe tip lesions can be a common clinical finding in cattle. The majority of toe tip lesions in the literature, which affect beef cattle have been termed a toe abscess. Case descriptions that involve the toe tip will be described.

Sick *et al* (1982) described feedlot calves that demonstrated gait abnormalities one day to four weeks after feedlot entry. This lameness often affected the hindlimbs, specifically the lateral claw, but could be found to affect all feet. One of the hallmark signs of this condition was lameness with no swelling of the distal limb. As the condition progressed soft tissue swelling started to develop on the plantar aspect of the distal limb, but there was limited improvement with antimicrobial or anti-inflammatory medications. Closer examination revealed that the apical region of the claw was worn, rounded off, and the sole was separated from the wall. When the apical region of the claw was removed, the underlying tissues contained either a hematoma or dry black material. It was recommended that affected animals be moved from a concrete to dirt floor surface; receive antimicrobial therapy to prevent systemic infection; and that the apical region be pared to facilitate drainage of the apical region of the claw. Despite treatment not all

animals recovered from this lameness. The authors postulated that common risk factors in disease development were transportation in an aluminum trailer with minimal bedding or cattle being maintained and handled on concrete surfaces. It was thought that mechanical trauma leads to abrasion and rasping of the claw, which is seen especially in hyper-excitable animals during overcrowding and handling that contributed to the lesions.

Miskimins (1994) reported a similar clinical scenario to Sick *et al* (1982) involving five unrelated feedlots in the mid-western United States. In this case, the feeder cattle developed a severe lameness three days to three weeks after feedlot arrival. Clinical signs ranged from abnormal wear of the hoof; separation of the hoof wall and sole at the white line; abscessation and necrosis of the pedal bone; arthritis; cellulitis; and elevated temperatures (Miskimins, 1994). It was also noted that mechanical trauma to the hoof could be an inciting cause due to sudden turning, standing for long periods of time during trucking, and other abrasive conditions that would injure the claw leading to this condition. Furthermore, it was postulated that soft hooves due to wet conditions and hyper-excitable behaviour may make animals at a higher risk of disease occurrence.

In a cross-sectional study, Smith and Brodersen (1998) evaluated severe lameness in feedlot cattle with a median of 17 days after arrival. In 28 cattle studied the most common external lesion was separation of the wall and sole at the white line, which accompanied an infection of the distal phalanx as the most common internal lesion. There did not appear to be any consistent distribution of lesions in the medial or lateral claws nor the right or left feet; however, there was excessive wear in the toe tip that was noted in the front feet. This study demonstrated that toe abscesses and other internal foot lesions are a consequence of claw damage.

Despite dairy cattle being confined for most of their life on concrete in milking parlours and sheds there are very few reports of toe tip lesions. However, dairy cattle can be afflicted by the same clinical signs as seen in beef cattle, but there are different names that describe such lesions.

One of the first reports of toe tip lesions was in Jersey cattle. Transit related lameness in a group of Jersey heifers was reported after animals were commingled within auction yards (Dewes, 1979). Many animals were penned together and held on concrete surfaces prior to transportation. It took ten days before the Jersey heifers experienced signs of lameness, which peaked at 13 days. The author reported the lameness was confined to the hindlimbs, in which, separation of the sole and wall, and pedal bone fractures were seen. This also highlights the impact of mechanical trauma and weight bearing forces on the claws in animals during or after transportation.

Mason *et al.* (2012) reported on a group of dairy heifers developing thin soles resulting from excessive hoof wear that lead to sole hemorrhages, ulcers, and notably toe abscesses. Roughly 150 Holstein-Friesian heifers were abruptly moved onto a concrete feed pad, holding yard, and rotary platform. Ninety percent of these heifers developed lameness within one to three weeks. The authors noted that these dairy heifers were nervous, agitated and reluctant to walk on the wet concrete while being mixed with adult dairy cows during this time. The authors suggested that the excessive horn wear in these heifers were due to prolonged contact times on concrete, combined with the agitated nature, and wet conditions that lead to thin soles and toe abscesses from apical white line separation.

Thin sole-induced toe ulcers matches the term toe abscess where the lesion is actually a consequence of sole thinning resulting in a separation of the apical sole away from the white line

(Sanders *et al*, 2009). Interestingly, the authors point out that thin sole-induced toe ulcers is a distinct lesion from white line disease and sole ulcers in dairy cows. In addition, the authors mention that the stage of lactation in which a cow develops TSTU is highest just after calving, specifically 1 to 15 days in milk; however, these lesions are found in all stages of lactation when compared to other claw lesions. Lastly, thin soles were shown to be a statistically significant risk factor for the development of thin sole-induced ulcers and sole ulcers that is likely substantiated due to wet environmental conditions.

Apical osteitis of the pedal bone has been described in a dairy cow as a result of excessive hoof trimming three weeks after the insult (Thompson, 1998). Clinically a small defect in the sole near the apex of the toe was undermined and missing. This Ayrshire cow had radiographic evidence of an osteitis and pathological fracture of the pedal bone; it is suspected that the two conditions were related. This case demonstrates that pedal osteitis can develop from an ascending bacterial infection through the sole or white line. The pedal osteitis and subsequent weakening of the pedal bone can also predispose to a pathological fracture, which may contribute to the severe lameness that is seen in these affected animals. It is suspected that excessive sole thinning due to aggressive hoof trimming and wet conditions that contribute to soft hoof horn were predisposing factors for the development of pedal osteitis in this dairy cow.

Kofler (1999) describes apical necrosis of the distal phalanx as a complication from a toe ulcer. Separations of the sole or cracks at the level of the white line are frequent entry points for bacteria that can be obtained from a thorough examination. It is suggested that due to the thin layer of corium and digital cushion in this anatomical area the ascending infection and involvement with the pedal bone can occur quite rapidly. The author reported that overzealous

hoof trimming, laminitis and traumatic injuries accounted for the majority of toe ulcers and apical necrosis of the distal phalanx.

1.4.2 THEORIES ON TOE TIP LESIONS

There are three current theories on the development of lesions in the condition now referred to as TTNS: 1) mechanical trauma to the claw, 2) pedal bone vascular disruption, and 3) sequelae to laminitis.

Sick *et al* (1982), Miskimins (1994), and Greenough (2007) hypothesized that toe abscesses result from abrasion, rasping, and trauma to the claw during transportation and processing of feedlot cattle. Biomechanically, there are weight load differences between the claws in the hindlimb, and greater weight is exerted on the lateral claw (van der Tol *et al*, 2002). This is supported by Murray *et al* (1996) which described the lateral claw is more likely than the medial claw to have claw lesions in the hindlimb as a result of over bearing weight. Therefore, this sudden turning and movement during transportation and processing of cattle can damage the apical white line, allowing for impaction of fecal material into the white line. Not only does facility design and transportation lead to mechanical trauma, but iatrogenic causes can lead to claw damage. Kofler (1999) and Thompson (1998) report that overzealous or incorrect claw trimming can lead to white line separation that manifests as pedal osteitis. It is hypothesized that the branches of the terminal arch in the distal limb can act as conduit for fecal bacteria to be carried into the bones and supporting structures in such a short period of time.

A second theory by Greenough (2007) postulated that toe abscesses could start from vascular and/or physiological disturbance to the pedal bone. The proper digital artery passes through the axial foramen as it forms the terminal arch. The location of this axial foramen is below the level of coronary band. Since walking will aid in blood pumping and passive movement by the arteriovenous anastomoses it is suggested that prolonged standing times place

excessive pressure on the axial foramen. This could result in disruption of the terminal arch leading to ischemia and necrosis of the pedal bone.

This vascular theory suggests that high pressure within the claw capsule during prolonged standing times contributes to hypoxia, which leads to rupture of the apical white line and allows for drainage. During periods of standing in auction yards or livestock trailers there could be hypostasis of blood in the distal limb. Since the distal extremity relies on blood flow through the arteriovenous anastomoses as the animal stands this flow could be impaired. Greenough (2007) has reported that when blood supply to the pedal bone is impaired ischemic necrosis can lead to a fracture of the apical pedal bone. This theory is suggested as some animals have no visible opening in the claw and hypothesize that lesion starts internally.

A third theory is that TTNS is a sequela of laminitis. Laminitis, by definition, is an acute degeneration of the laminae of the claw that results in pedal bone rotation (Radostits *et al*, 2007). There are acute, subclinical, and chronic manifestations. In cattle, phalangeal rotation has been seen in acute and chronic laminitis (Andersson and Bergman, 1980). Laminitis can be secondary to ruminal acidosis, which is due to irregular feeding patterns and sudden changes in diets. Since animals that have recently entered a feedlot experience nutritional stress it is hypothesized that the rotation of the pedal bone can damage the corium that results in a coriosis, and allows for apical white line breakdown. It has been suggested by Greenough *et al* (1990) that osteopathy of the apex of the pedal bone is more common in calves than yearlings due to dietary changes.

1.5 OTHER CAUSES OF FEEDLOT CATTLE LAMENESS

The toe tip region is only one location that will cause lameness in feedlot cattle. Other conditions that can lead to lameness in feedlot cattle will be discussed.

1.5.1 INTERDIGITAL NECROBACILLOSIS

Interdigital necrobacillosis is caused by *Fusobacterium necrophorum* and less commonly *Prevotella melaninogenica* (Radostits *et al*, 2007). *Fusobacterium necrophorum* is found in the environment. An abrasion or breach in the interdigital skin is required for the bacteria to enter (Radostits *et al*, 2007). Clinical signs consist of symmetrical swelling in the interdigital space that exposes necrotic material, and a fever may be present (Radostits *et al*, 2007). This is one of the most common lameness diagnoses in a feedlot but is often misdiagnosed (Kruse *et al*, 2013).

1.5.2 DIGITAL DERMATITIS

Digital dermatitis is an acute inflammatory condition that affects the dermis of the heel bulb which can extend to the interdigital cleft (Greenough, 2007). The etiological agent is *Treponema* spp.. Environmental management is important in disease control as the pathogen is transmitted through wet, poorly drained housing conditions. Clinically, there is no digital swelling or fever, but an erosive, alopecic, painful plaque mostly seen at the heel bulb. Digital dermatitis is a growing concern in dairy herds, in addition, to feedlots that feed dairy steers.

1.5.3 MYCOPLASMA BOVIS ASSOCIATED LAMENESS

In Canada *Mycoplasma bovis* has been found to affect young cattle between six to eight months of age (Radostits *et al*, 2007). This bacterial pathogen commonly affects feedlot cattle within a few weeks after feedlot arrival. Clinical signs range from fibrinonecrotic bronchopneumonia, polyarthritis, and otitis media. This condition can be referred to as a chronic pneumonia-polyarthritis syndrome. Lameness can be attributed to a polyarthritis and tenosynovitis that can affect any joint. This condition can be unresponsive to antimicrobial therapy.

1.5.4 HISTOPHILUS SOMNI ASSOCIATED LAMENESS

Histophilus somni is a bacteria that affects cattle most commonly between six to twelve months of age (Radostits *et al*, 2007). In cattle, a variety of clinical manifestations can result from infection that includes septicemia, thrombomeningoencephalitis, pleuropneumonia, myocarditis, mastitis, reproductive failures, otitis media, and polysynovitis. In Canadian feedlots morbidity and mortality affects animals during the first five weeks of the feeding period; however, is more common three weeks after feedlot arrival. Synovitis can affect any joint but is more common in the stifle and tarsus resulting in lameness and recumbency.

1.5.5 BOVINE VIRAL DIARRHEA VIRUS AND LAMENESS

Bovine viral diarrhea virus (BVDV) is a significant economic pathogen in feedlot cattle (Radostits *et al*, 2007). BVDV can lead to a multitude of clinical signs ranging from fever, diarrhea, oral lesions, thrombocytopenia and reproductive failures. In feedlot animals seroconversion to BVDV occurs in the first few weeks of the feeding period due to persistently infected animals with BVDV (Radostits *et al*, 2007). One consequence of BVDV infection is mucosal disease. Mucosal disease often develops when the affected animal is between 6-24 months of age. Lameness associated with mucosal disease consists of erosions at the coronary band and interdigital necrosis (Taylor *et al*, 1997; Radostits *et al*, 2007). The morbidity rate of mucosal disease is estimated to be low and the mortality rate is high. It is suggested there may be synergism between BVDV, *Mycoplasma bovis* and bovine respiratory pathogens (Radostits *et al*, 2007).

Vasculitis and arteritis are defined as inflammation of veins and arteries, respectively (Knottenbelt, 2002). Infectious causes of vasculitis include viral and bacterial etiologies. Non-infectious causes of vasculitis consist of immune-mediated, trauma-induced, and pharmacological-induced conditions. In feedlot cattle it is not uncommon to have a transient

vasculitis due to *Mannheimia haemolytica* or *Mycoplasma bovis* infections (Dr. Ted Clark, personal communication, October 2013).

1.5.6 PODODERMATITIS ASEPTICA DIFFUSA (LAMINITIS)

Laminitis, by definition, is an acute degeneration of the laminae of the hoof (Radostits *et al*, 2007). Laminitis is one of the most common conditions affecting the foot of beef and dairy animals (Stokka *et al*, 2001). The development of laminitis is often seen where aggressive, high concentrate diet is fed. This leads to degeneration, necrosis, and inflammation of the dermal and epidermal laminae that allows for the pedal bone to separate from the hoof wall (Stokka *et al*, 2001). Consequently, the rotated pedal bone will put pressure on the solar corium that creates hemorrhages, discoloration, and possible penetration through the sole. There are three forms of laminitis: acute, subclinical, and chronic. Stokka *et al* (2001) mention that subclinical laminitis can go unrecognized until late in the feeding period.

1.5.7 MUSCULOSKELETAL TRAUMA

Injuries to feedlot cattle are one of the most commonly misdiagnosed problems encountered by treatment crews (Stokka *et al*, 2001). Traumatic injuries would include buller injuries, fractures, sprains, strains, and lacerations. Of all traumatic injuries 70 percent occurred in the hindlimbs when compared to 30 percent which occurred in the forelimbs. The majority of injuries are as a result of cattle handling, facility design and maintenance, which suggests that musculoskeletal injuries could be preventable.

1.5.8 ERGOTISM

Classical ergotism in cattle can cause peripheral gangrene after ingestion of ergots produced by a fungus *Claviceps purpurea* (Radostits *et al*, 2007). The fungus commonly invades rye and less commonly grasses. Poisonings are often seen during or after warm, wet seasons which favours fungal growth but can be seen throughout the year. Clinically, the distal

extremities, including the hindlimbs, tail and ears are affected by gangrenous necrosis. The vascular damage as a result of the ergots can allow lameness to be the first sign noticed as early as 10 days after feed consumption but most animals show signs two to four weeks after exposure. Despite tissue destruction the lesions are generally not painful yet can result in the animal to be recumbent. Treatment is not effective. Prevention is focused on dietary control of limited ergot intake.

1.6 CATTLE BEHAVIOUR AND LAMENESS

Given the likely multifactorial risk factors for toe tip lesions it is possible that animal's natural behavior, previous human experiences, and current cattle handling techniques can predispose to toe tip lesions. Clackson and Ward (1991) looked at the stockman's attitude and incidence of lameness in dairy cattle. Not surprisingly, a stockman's patience directly influenced the number of lame cows. An impatient stockman was more likely to crowd and push animals together that result in cattle which suddenly turn in order to avoid the individual. In addition, the quality and maintenance of the floor also contributes to the degree and incidence of lameness. This research suggests that patient employees and improved footing decreases lameness.

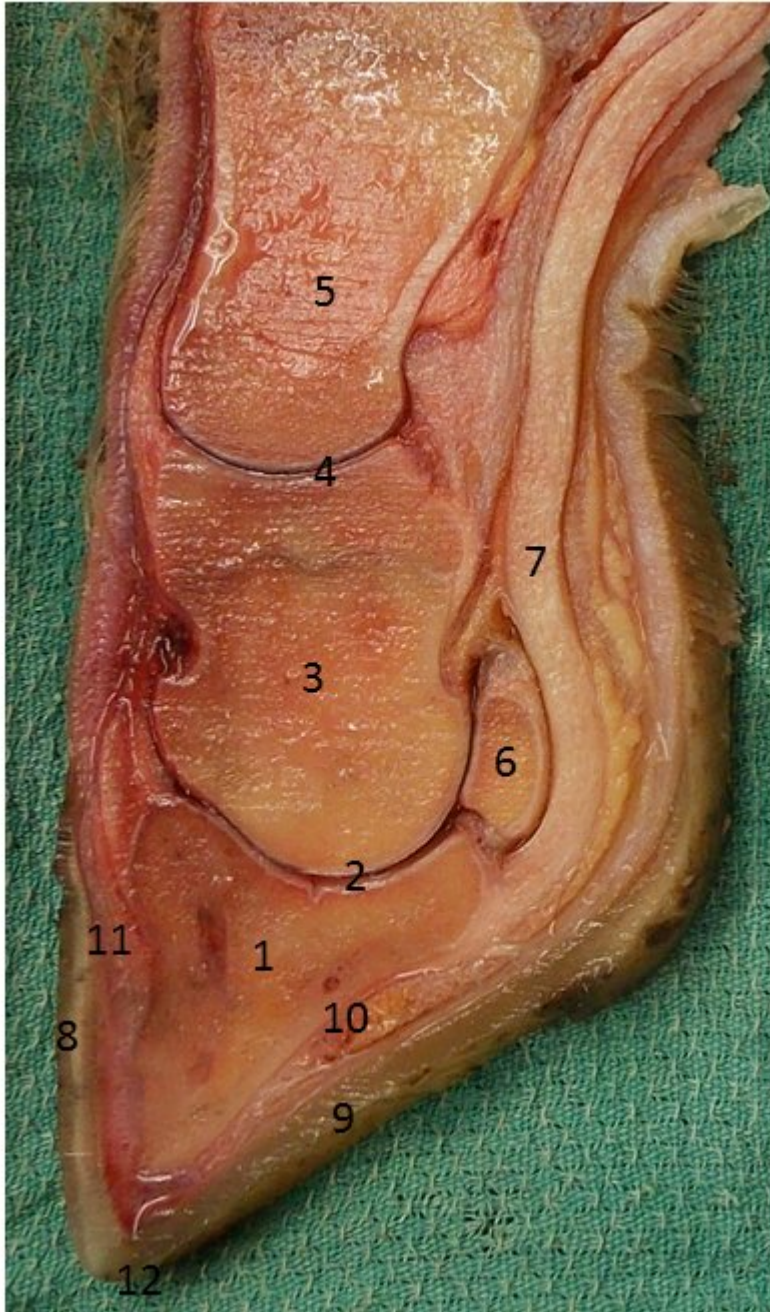


Figure 1.1: Anatomy of the bovine distal limb.

1=distal phalanx; 2=distal interphalangeal joint; 3=middle phalanx; 4=proximal interphalangeal joint; 5=proximal phalanx; 6=navicular bone; 7=deep digital flexor; 8=dorsal hoof wall; 9= sole; 10= solar corium; 11= laminae; 12=white line



Figure 1.2: Vasculature system in bovine distal limb (Juliane Deubner, DVM; 2014).
1= proper digital artery, 2= terminal arch, 3= branches of the terminal arch

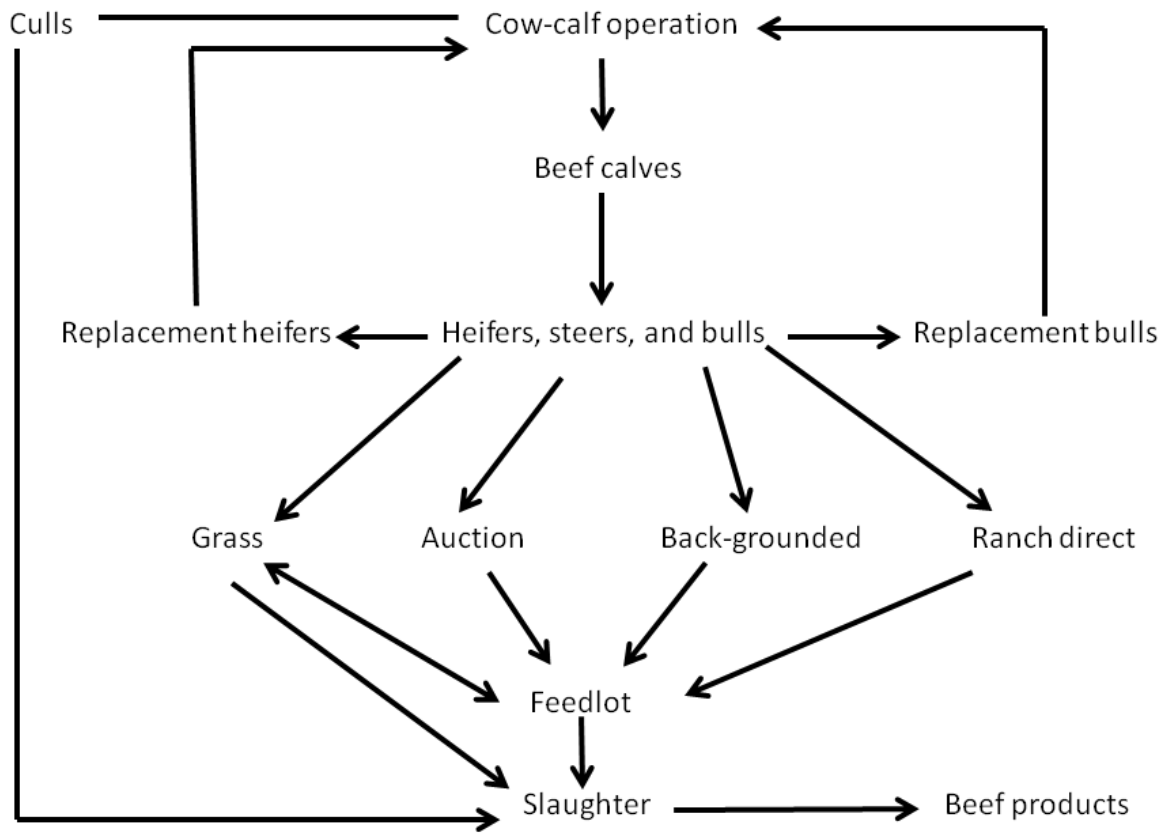


Figure 1.3: Flowchart of Canadian beef production.

1.7 RESEARCH OBJECTIVES

1. To use clinical examinations, imaging modalities, and necropsy findings to aid in the description, classification, and characterization of toe tip lesions.
2. To describe the epidemiology of toe tip necrosis syndrome (TTNS) in feedlot cattle.
3. To evaluate risk factors for toe tip necrosis syndrome.

CHAPTER 2: CASE DEFINITION FOR TOE TIP NECROSIS SYNDROME IN FEEDLOT CATTLE

2.1 INTRODUCTION

Field veterinarians in western Canada report clusters or groups of feedlot calves that arrive into the feedlot and develop lameness early in the feeding period, particularly in the hindlimbs, that are difficult to treat. The clinical signs are unlike the more common causes of lameness, such as interdigital necrobacillosis (“foot rot”), laminitis, and soft tissue injuries. The paucity of published articles on feedlot cattle lameness could in part be related to the lack of concise case definitions. Researchers and veterinary practitioners in western Canada have given this arrival related condition a number of different names: P3 necrosis, toe abscesses, apicus necrotica, apical pedal bone necrosis or toe necrosis. These names and descriptors of toe tip lesions are likely based on anecdotal experiences and published case reports.

One of the first published reports of toe tip lesions described the condition in dairy cattle. Transit related lameness in a group of 411 Jersey heifers occurred after the animals were commingled within auction yards (Dewes, 1979). Many animals were penned together and held on concrete surfaces prior to transportation, similar to what feedlot cattle in western Canada experience prior to feedlot entry. It took ten days before these Jersey heifers experienced signs of lameness, which peaked at 13 days. The author reported the lameness was confined to the hindlimbs, in which, separation of the sole and wall was seen, in addition to pedal bone fractures.

Sick *et al* (1982) published the next report that described animals with toe tip lesions developing one day to four weeks after feedlot entry. This lameness often affected the hindlimbs, specifically the lateral claw, but could be found to affect all feet. One of the hallmark signs of this condition was lameness, yet there was no swelling of the distal limb. The lack of swelling caused the lameness condition to be frequently misdiagnosed as interdigital necrobacillosis, which resulted in treatment delays and a poor prognosis. As the condition progressed soft tissue

swelling started to develop on the plantar aspect of the distal limb, and there was limited improvement with antimicrobial or anti-inflammatory treatments.

On closer examination the toe tip (apex) region of the claw was worn, rounded off, and the sole was separated from the wall, allowing for an entry port into the claw capsule (Sick *et al*, 1982). The authors noted that once the apical region of the claw was removed the underlying tissues contained either a hematoma or dry black material. The authors recommended that affected animals be moved from a concrete to a dirt floor surface; receive antimicrobial therapy to prevent systemic infection; and that the apical region be pared to facilitate drainage of the apical region of the claw.

Not all animals recovered from this lameness. Despite treatment, some cattle became anorexic, gaunt, and died. Post mortem examination of these cattle revealed vegetative-type lesions within the vasculature system that embolized to the kidneys, liver, lungs, and heart (Sick *et al*, 1982).

Sick *et al* (1982) postulated that common risk factors in disease development were transportation in an aluminum trailer with minimal bedding or cattle being maintained and handled on concrete surfaces. It was thought that mechanical trauma to the apical sole and dorsal hoof wall leads to abrasion and rasping of the claw, which is seen especially in hyper-excitable animals during overcrowding and handling.

The next case report that described the same condition was by Miskimins (1994). The author reported a similar clinical scenario to Sick *et al* (1982) wherein five unrelated feedlots in the mid-western United States had feeder cattle develop a severe lameness three days to three weeks after feedlot arrival. Clinical signs ranged from abnormal wear of the hoof; separation of the hoof wall and sole at the white line; abscessation and necrosis of the pedal bone; arthritis;

cellulitis; and elevated temperatures. It was hypothesized that mechanical trauma to the hoof could be an inciting cause due to sudden turning, standing for long periods of time during trucking, and other abrasive conditions that would injure the claw leading to this condition. Furthermore, soft hooves due to wet conditions and an animal's hyper-excitability behaviour may make animals a higher risk for disease occurrence.

Based on these three articles and practitioner's experiences it is suggested that cases of toe tip lesions can cluster together and likely common risk factors are present for all individual animals; particularly, environmental, behavioural, and stockmanship factors.

The objective of this chapter was to develop a case definition for an arrival-related lameness that affects the toe tip, which was observed in western Canadian feedlot cattle. Based on clinical findings, imaging modalities, and necropsy specimens a descriptive case definition, and subsequently a more specific name, Toe Tip Necrosis Syndrome, is introduced.

2.2 MATERIALS AND METHODS

When the project started in September, 2012 the purpose was to investigate a condition called "P3 necrosis". P3 necrosis was a term used by practitioners to describe recently arrived feedlot calves that developed a severe lameness. Further clinical examination of affected calves showed a worn toe tip and white line separation; necropsy evaluation revealed a necrotic distal phalanx (P3). A lack of epidemiological information was known about P3 necrosis and hence the intention was to further investigate this condition. Upon further discussion with practitioners and a literature review other names, for example "toe abscesses", were found to describe a condition very similar to P3 necrosis. It quickly became evident that there was not a standardized case definition for P3 necrosis. Traditional epidemiological approaches that included field investigations, clinical and necropsy examinations were warranted to identify, characterize and describe this condition that causes animals to become lame soon after feedlot arrival.

2.2.1 EXAMINATION OF ANIMALS

Two field trips were made to Alberta feedlots in October, 2012 to examine lame calves after feedlot arrival. Specific animals that had hindlimb lameness with minimal distal limb swelling were chosen by the feedlot veterinarian or treatment crew for examination. Animals were restrained in a cattle chute and their feet were elevated for closer examination. Photographs were taken of claw lesions. Hoof testers were applied to the claw to determine the location of a pain response or sensitivity in a certain location inside the claw. A positive painful reaction was when the animal suddenly pulls or moves the claw away from the hoof tester. Three calves that had a poor prognosis for recovery were euthanized and a systematic necropsy was performed by the feedlot veterinarian.

2.2.2 SAMPLE IDENTIFICATION AND COLLECTION

During October to December 2012, three feedlot veterinary practices in Alberta were contacted and asked to participate in a case-control study designed to investigate toe tip lesions in feedlot calves. Each practice received a letter instructing them to provide the claw sectioned at the metatarsophalangeal joint or coronary band distally. Formalized cardiac muscle, specifically a cross-section of the septum, and a skin sample from case and control animals were to accompany the claw. A case was defined as an animal having pathology consistent with necrosis that involved the distal phalanx bone (P3), and a control animal had no pathology that involved the distal phalanx bone. A control animal was the next animal to be necropsied, which could be from a different lot than the case animal, but similar in days on feed, weight, and age class as the case animal. A booklet accompanying the letter included images of white line separation at the toe tip and a sagittally sectioned foot that demonstrated necrosis of the distal phalanx, which is seen in Appendix B. White line separation included any non-union of the solar horn and dorsal hoof wall. Referring to Figure 2.1 this lesion would be located in zones 1. The separation could

include a localized, small defect in the apical white line to a missing piece of solar horn.

Participants were asked to collect cardiac, skin, and associated tissues that had pathology, such as tendons, liver, and lung samples. All tissues were preserved in a 10% formalin solution.

2.2.3 RADIOGRAPHIC IMAGING

Intact bovine feet sectioned at mid-metatarsus were imaged with radiography (Min-Xray HF90/30) in a dorso-plantar technique. Computed tomography (Aquilion Toshiba 16 Slice CT Scanner) images were taken with 12 frames per second from the metatarsophalangeal joint distally. All claws were sectioned with a manually operated band-saw (BIRO 44SSFH Meat Saw) to confirm pathology of the pedal bone.

2.3 RESULTS

2.3.1 CLINICAL FINDINGS

Clinical signs in calves presumptively diagnosed with toe tip lesions included varying degrees of lameness in the hindlimbs and less commonly the forelimbs. A toe-touching lameness was seen as the animal would be hesitant to place body weight on the affected limb. However, when the animal ambulated there was notable joint mobility. During gait examination there were two animals that were excessively excited, anxious, and very alert towards the handler. Body condition score ranged from slight muscle atrophy, tail head and ribs visible (BCS 3/9) to slight fat over the ribs and hip, and no outline of the spine (BCS 5/9).

As the animal was restrained in a hydraulic chute and the limb elevated by a rope there were abrasions, scrapes, and irregularities seen and palpated along the abaxial (outer margin of claw) and apex (tip) of the claw. In addition to the claw irregularities there was a flap of sole that was found to not be attached to the dorsal hoof wall at the location of the white line. Figure 2.2 illustrates a well demarcated area that has a fragment of sole missing that exposed the underlying corium. The sole-dorsal wall gaps were consistently found at the apex of the claw of the animals

examined. The separation at the white line allowed for an opening where a probe could be inserted into the claw along the epidermal lamellae, dorsally, or solar corium, ventrally. In two animals as digital pressure was applied to the claw capsule white, mucopurulent discharge could be expressed. When digital hoof testers were applied to the claws there were some animals that had a positive response, but other animals had visible gross lesions with no positive response.

2.3.2 RADIOGRAPHIC FINDINGS

Radiographic findings of postmortem specimens of toe tip lesions in early case animals showed apical osteolysis of the distal phalanx as shown in Figure 2.3. Not surprisingly, Figure 2.3 also demonstrates soft tissue swelling at the location of the middle phalanx. Figure 2.4 shows a computed tomography 3-dimensional plantar-dorsal image of a foot with diffuse, irregular projections of callus bone formation along the plantar aspect of the distal phalanx and navicular bone. These callus projections are also noted along the lateral margin of the middle phalanx. Figure 2.5 shows a computed tomography image of air, which is depicted as black areas, inside the claw capsule, distal phalanx, and supporting soft tissues. Also there is a subluxation as indicated by the lateral displacement of the distal phalanx bone. Collectively, the CT image in Figure 2.6 shows osteolysis and invasion into the distal interphalangeal joint that extends into the distal margins of the middle phalanx in addition to soft tissue enlargement.

2.3.3 PATHOLOGICAL FINDINGS

There was a total of 82 case and 66 control (non-affected) submissions. The earliest pathological lesion found was a breach in the claw capsule at the apical white line that was impacted with organic material as shown in Figure 2.7. An estimated width of 2mm to 5mm separation of sole and dorsal hoof wall consistently occurred at the apical white line when compared to other locations of the claw. As the separation became larger the embedded organic material progressed along either the solar corium or epidermal lamellae, or both. Tissues that

surrounded the organic material were diffuse, poorly demarcated, and red to purple in color. Other pathological findings, also seen in Figure 2.7, included a localized, well demarcated, white to gray, friable appearance at the apical distal phalanx with or without a pathological fracture. The lesion seen at the apex then progressed to the central location of the distal phalanx. In some specimens, the distal interphalangeal joint and navicular bursa contained white, friable, caseous material. In addition, the superficial and deep digital flexor tendons had a yellow, glistening appearance, with ecchymotic hemorrhages disseminated throughout the tendons. Control animals did not have these pathological findings.

2.4 DISCUSSION

Toe tip necrosis syndrome (TTNS), by definition, is a separation in the apical white line with tissue necrosis and clinical lameness. The *syndrome* includes an array of sequelae such as pedal (P3) osteitis, middle (P2) and proximal (P1) phalangeal osteomyelitis, tendonitis, tenosynovitis, cellulitis, and embolic pneumonia.

In reference to the claw zone map in Figure 2.1 the primary focus of interest is zone 1. This is the location of the apical (toe) white line in the claw. Based on clinical and necropsy examinations the damage and origin of insult occurs at this site. Therefore, toe tip is the best descriptor of the location of this condition. According to *Saunders Comprehensive Veterinary Dictionary* the definition of necrosis is "the morphological changes indicative of cell death caused by enzymatic degradation"; and syndrome is defined as "a combination of clinical signs resulting from a single cause or so commonly occurring together as to constitute a distinct clinical picture" (Blood and Studdert, 1999).

It is important to note that apical white line separation without tissue necrosis, as evident in the first picture of Figure 2.7, does not constitute a TTNS diagnosis. The presence of tissue necrosis, for example coriosis, coriitis, pedal osteitis, will contribute to clinical lameness and as

such allows for a more specific case definition. The reason that tissue necrosis was added to the case definition is that apical white line separation may develop in the feedlot animal, but may not result in lameness. This may explain anecdotal reports that some animals with apical white line separation recover from the condition without treatment. Thus, if necrosis occurs to the underlying claw structures, lameness is present, and therefore TTNS is diagnosed.

In this study, the case animals that were examined had moderate to severe pathology of underlying claw structures in addition to apical white line separation. However, the first picture in Figure 2.7 was identified and presumed to be an early case or the start of a lesion. Further investigation into the severity of lesions and the timeline for development would be indicated.

Sick *et al.* (1982) described purulent or dry black material found at the apical region of the claw when necropsied limbs were sagittally sectioned. This was also seen in case specimens. Ante-mortem examination involved trimming the apex of the claw or exploration of the lesion with a hoof knife, which often uncovered fecal material compressed along the solar corium or epidermal laminae. It has been hypothesized that the non-union in the wall and sole act as a hinge while the animal is walking. The “hinge-effect” allows the wall and sole to separate or open and close, and as such, the animal’s body weight will force organic matter and fecal material into this space. The presence of fecal material was evident on necropsy examination and sagittal sections as seen in the second picture of Figure 2.7. It is plausible that pressure necrosis and ischemia as a result of the fecal material along the corium will contribute to further pathology. Or there could be an underlying vasculitis or impediment to the corium that continues as a pedal osteitis rather than white line disease (WLD).

Desrochers *et al* (2001) reports 80-90% of lameness will occur distal to the fetlock so exploration of the claw would be a reasonable step to identify the source of lameness. However,

during early stages of TTNS there is minimal swelling in the distal limb. When hoof testers were applied to the claws of TTNS cases there was a variation in the animal's reaction. Some animals had a consistent positive response with the hoof testers while other animals did not. The lack of repeatability detected with the hoof testers could be due to the presence of necrosis and lack of pain fibers present in the toe, inconsistent pressure applied by the examiner, or the hoof testers did not apply as much discomfort as the disease process itself.

Radiographic evaluation showed the extent of pedal osteitis. Computed tomography (CT) supported the findings where a breach in the claw capsule was present along with periosteal bone reactions of the pedal bone. Figures 2.3 and 2.6 show considerable pathology and osteolysis of the pedal bone that ascends toward the distal interphalangeal joint. Whereas Figure 2.6 shows a CT scans of soft tissue enlargement and septic arthritis of the distal interphalangeal joint that can be a continuum of this condition. Advanced imaging (radiography, computed tomography) was used to investigate and describe these lesions; however, is not needed for definitive diagnoses of TTNS. Nonetheless imaging findings in this study agree with Kofler (1999) that visible toe lesion does not correlate very well with radiographic signs of pedal bone osteolysis.

There was varying stages of pathology associated with the pedal bone. In some cases one-third of the apex was affected whereas in other cases the entire pedal bone was affected. This degree of pedal osteitis begs the question why does this process happen so quickly? One hypothesis is that the intricate nature of the vasculature system in the distal limb acts as a conduit for systemic spread. That is, given the lack of collateral circulation in the toe, any affected branch of the terminal arch can re-circulate the pathogens into deeper structures of the limb. A second hypothesis is that the breakdown in the barrier of the corium could allow an inflammatory process in the apex to proceed to a pedal osteitis within a short period of time. This

is shown as an infected pedal bone can ascend into the distal interphalangeal joint, navicular bursa, and middle (P2) phalanx. In addition, other secondary complications such as unilateral or bilateral hindlimb cellulitis, as shown in Figure 2.8, and embolic pneumonia can occur which gives the animal a poor prognosis.

TTNS, in contrast to other descriptors, was based on location of insult and the pathological disease process. Toe abscess is another name that has been used for this condition. Toe abscesses are merely a description of the pathological process that occurs in the claw. Due to the anaerobic environment within the claw capsule and the presence of anaerobic bacteria abscesses will develop. However, in order for a toe abscess to start there needs to be a breach in the claw capsule for the anaerobic bacteria to enter. TTNS and toe abscess have similarities that the same location of the claw is affected yet an abscess is only one stage in the TTNS spectrum.

P3 necrosis implies pedal osteitis and therefore would be an inappropriate name for this condition. After looking at sagittal sections, pedal osteitis would be a consequence of apical white line separation and coriosis. When multiple sagittal sections of the same foot were examined there was a draining tract that connected several areas of pedal osteitis. In contrast, when only one sagittal section was examined it appeared that there could be an isolated area of pedal osteitis with normal bone surrounding that area of necrosis. However, closer examination of multiple sections revealed a draining tract that originated from the apex of the claw. Therefore, as many tissues are affected by this condition and not solely the pedal bone the term P3 necrosis would be an inaccurate descriptor.

Thin sole induced toe ulcers (TSTU) are typically erroneously classified as white line disease as ulcers typically occur in the sole which is zone 5 in the claw zone map (Figure 2.1). An important observation is that toe ulcers (zone 5) occur in the sole where TTNS occurs in the

toe (zone 1). It may be possible that thinning of the apical toe and sole are contributing causes for TTNS but there is a difference in the location of lesions.

White line disease (WLD) is a condition that affects zones 2 and 3 in the claw zone map (Figure 2.1). WLD is similar to TTNS where lesions are often found in the lateral claw of the hindlimb. Greenough (2007) reports that WLD is the most common complications associated with subclinical laminitis. White line separation can routinely be seen in animals without any complications, but when the separation is embedded with foreign material (i.e.: stones) abscesses develop that contribute to lameness. The main difference between WLD and TTNS are that lesions are seen at different locations in the claw.

Current theories on TTNS pathogenesis have been hypothesized and include mechanical trauma to the claw, vascular disturbances to the pedal bone, and a sequelae to laminitis. Looking further into the theories was not an objective of this chapter; however, it is important to consider how these clinical and pathological findings can relate to the current theories.

Based on the lack of consistent nomenclature for toe tip pathology in feedlot cattle a specific and universal name was needed for this condition. Toe tip necrosis syndrome is a definition that includes any clinically lame animal with tissue necrosis and apical white line separation. This concise case definition will allow researchers, veterinary practitioners, and feedlot operators to accurately describe and diagnose animals, and in turn, prevent or reduce the severity of these lesions.

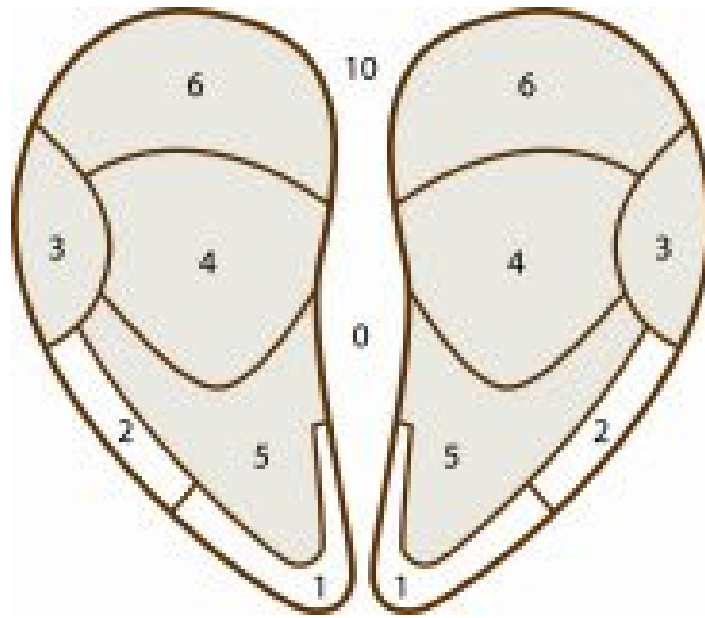


Figure 2.1: Claw Zone Map (Greenough *et al*, 1997).

1= white zone at the tip, 2= abaxial white zone, 3= abaxial wall-heel junction, 4= sole-heel junction, 5= apex of the sole, 6= heel; 0= interdigital space, 10= heel bulb



Figure 2.2: Apical white line separation in zone 1.



Figure 2.3: Radiographic evaluation of apical pedal bone osteolysis and soft tissue swelling.

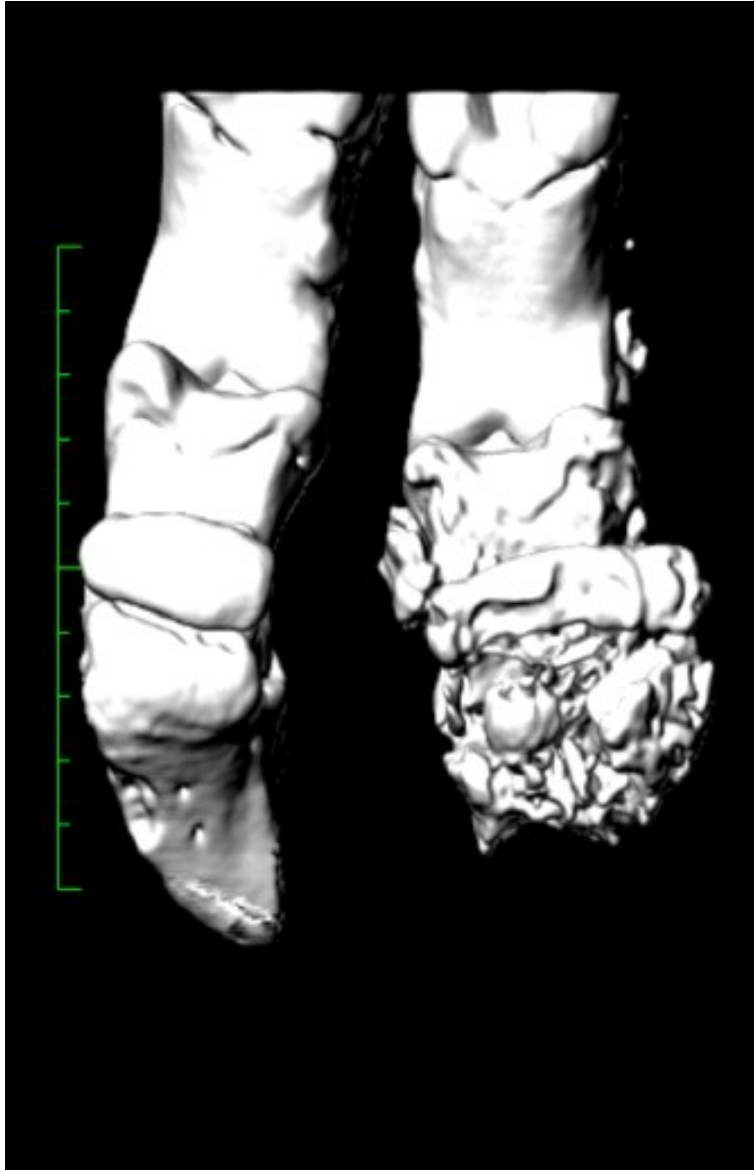


Figure 2.4: Computed tomography scan that illustrates osteolysis and bone remodeling.

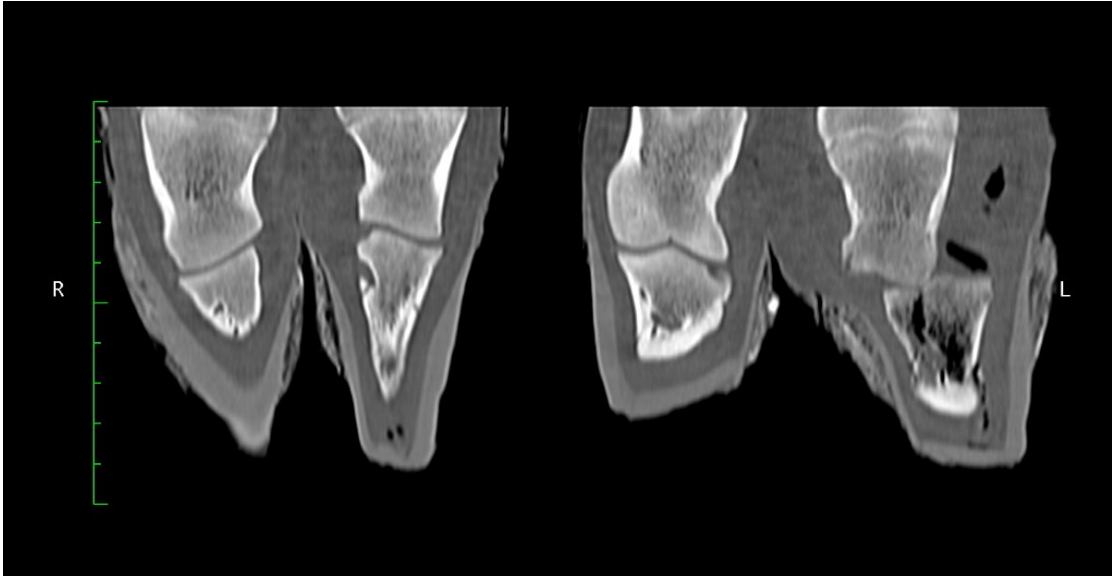


Figure 2.5: Computed tomography scan that illustrates pedal bone sequestrum formation and subluxation.

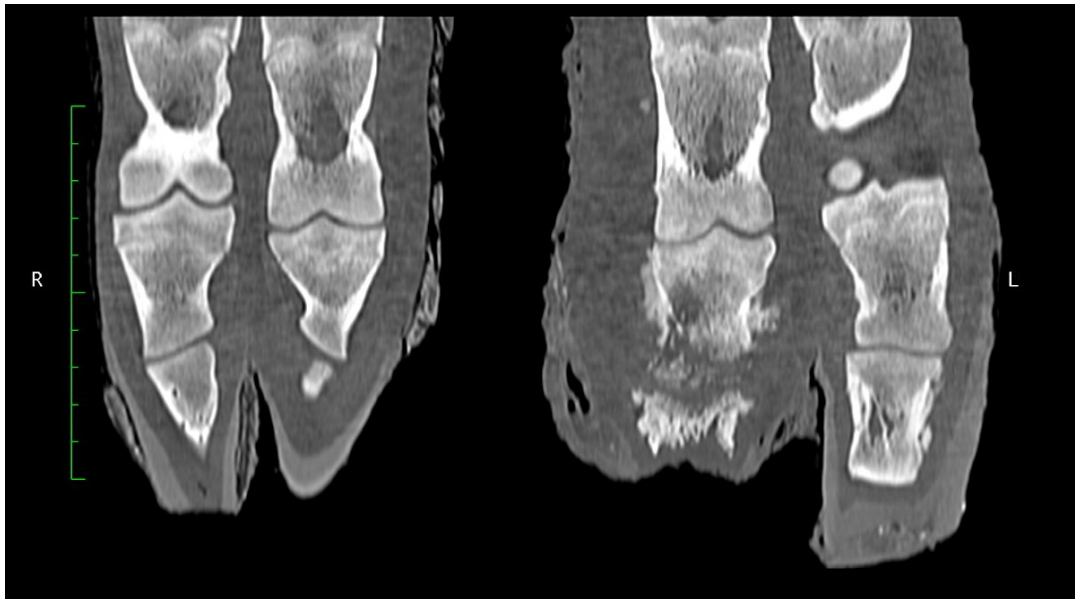


Figure 2.6: Computed tomography scan that demonstrates pedal osteitis, osteolysis and ascent into the distal interphalangeal joint.



Figure 2.7: Sagittally sectioned distal limbs which illustrates apical white line separation, followed by apical white line separation and tissue necrosis, followed by apical white line separation, pedal osteitis, and distal interphalangeal septic arthritis.



Figure 2.8: Bilateral hindlimb cellulitis secondary to toe tip lesions.

CHAPTER 3: RETROSPECTIVE DESCRIPTIVE EPIDEMIOLOGY OF TOE TIP NECROSIS SYNDROME IN FEEDLOT CATTLE IN WESTERN CANADA

3.1 INTRODUCTION

Classic epidemiological principles to investigate a new disease begin with descriptive epidemiology (Dohoo *et al.*, 2009). This approach puts the disease of interest into perspective in terms of morbidity and mortality, which highlights potential risk factors and hypotheses.

Toe tip necrosis syndrome (TTNS) is a new term for an old disease that describes separation of the apical white line of the claw with tissue necrosis and clinical lameness. This term encompasses complications such as pedal (P3) osteitis, middle (P2) and proximal (P1) phalangeal osteomyelitis, tenosynovitis, cellulitis, and embolic pneumonia.

Previous case reports of toe abscesses, which are descriptively similar to TTNS, not only have described the condition very well but have also provided some epidemiological features. For example, feedlot animals are affected with a severe lameness one day to three weeks after feedlot arrival (Sick *et al.*, 1982; Miskimins, 1994). It has been reported the morbidity and mortality rates in groups of animals can be high (Miskimins, 1994). In addition, cases have been documented between December and March.

Despite previous case reports there have been no formal studies that can confirm these epidemiological findings. Questions that still remain unanswered about this condition are: does the disease have a gender or age predilection; does this condition have the propensity to cluster; what is the time course for disease development; and is there a seasonal predilection? A formal descriptive epidemiology study can answer these questions as to whether the disease affects a certain age, gender, and source of animals. Veterinary practitioners and researchers require more descriptive data on TTNS to generate hypotheses on pathogenesis, disease prevention, and control. The objective of this study was to retrospectively describe the epidemiology of toe tip

necrosis syndrome (TTNS) in feedlot cattle in western Canada for the years 2007 to 2012, inclusive.

3.2 MATERIALS AND METHODS

Feedlot Health Management Services (FHMS) in Okotoks, Alberta, Canada is an independent veterinary feedlot consulting practice that specializes in providing professional expertise to the feedlot sector. FHMS accomplishes this service by providing herd health services through computerized-records, on-farm visits, and conducting clinical research for their clients. Their computerized record-keeping system allows FHMS to track every animal in a health management system. These data are archived for future use. From their archived data two separate analyses were performed to retrospectively describe the disease and to understand if the disease clusters by “lot”.

3.2.1 CASE SERIES STUDY

FHMS was contacted to provide retrospective cases of mortalities with toe tip lesions and epidemiological variables from their archived data. The case definition for FHMS database included soft tissue necrosis at the toe tip, and/or pedal bone necrosis with or without a pathological fracture, and/or ascending cellulitis originating from the affected foot of necropsied feeder cattle. All animals in this database had a necropsy overseen by an experienced veterinarian and the disease entity was deemed the most likely cause of death. As such, there was a degree of confidence in that cases provided were indeed toe tip lesions and not other causes of lameness. Variables in the database were arrival date, days on feed at first treatment for toe tip lesion, death date, days on feed at death, arrival weight, necropsy weight, age class, and source of animals (auction, ranch direct, back-ground, grass) prior to feedlot entry. Age class (calves, yearlings) were classified by feedlot personnel when animals arrived to the feedlot. The source of animals was recorded by feedlot employees as to where the animals were purchased.

The database was organized in Microsoft Excel (Microsoft Office, v.15, Microsoft Corporation, Redmond, WA, USA). All descriptive statistics were calculated using Microsoft Excel and a statistical program (SPSS, v. 19, SPSS Inc., Chicago, IL, USA). The *P-value* was set at 0.05. An analysis of variance (ANOVA) on the days on feed until death yielded significant variation among sources of cattle ($P < 0.001$). A post hoc Tukey test showed the days on feed until death did not differ significantly between auction and grass derived cattle ($P = 0.59$) or between auction and ranch direct cattle ($P = 0.97$). However, there was a significant difference on the days on feed until death between auction and back-grounded cattle ($P < 0.001$). There was a significant difference in the days on feed until death between grass and back-grounded cattle ($P < 0.001$) but no difference between grass and ranch direct ($P = 0.67$). The post hoc analysis also found no significant difference between the days on feed until death between back-grounded and ranch direct cattle ($P = 0.06$). An analysis of variance (ANOVA) on the days on feed until death yielded significant variation over the five years (2008-2012) ($P < 0.001$). A post hoc Tukey test showed the days on feed until death did not significantly differ between the years 2008 and 2009 ($P = 0.07$) nor between the years 2008 and 2010 ($P = 0.10$), but did significantly differ between the years 2008 and 2011 ($P = 0.04$) and between 2008 and 2012 ($P < 0.001$). There was no difference in the days on feed until death between the years 2009 and 2010 ($P = 0.99$) or 2009 and 2011 ($P = 0.94$) but there was a significant difference between 2009 and 2012 ($P < 0.001$). The days on feed until death did not significantly differ between the year 2010 and 2011 ($P = 0.97$) but there was a significant difference between 2010 and 2012 ($P < 0.001$). The post hoc analysis did find a significant difference between the days on feed until death between the years 2011 and 2012 ($P < 0.001$).

3.2.2 LOT PREVALENCE STUDY

An electronic database of lot level prevalence of toe tip lesions between January 1 and December 31, 2012 was obtained from FHMS. The lot level database only spanned one year in contrast to the retrospective database which contained six years of data. This database included 48 feedlots for TTNS to see if one “lot” had a positive necropsied case. A positive lot was one or more animal(s) diagnosed at necropsy with toe tip lesion. A “lot” represented a financial entity from a cattle seller. Therefore, a “lot” of cattle could represent a pen of animals, but most likely, corresponds to multiple lots with a pen. Only lot-level data that contained 100 animals or greater were included in the database.

The total cattle number in each lot was not provided in an effort to protect client confidentiality. Only percentages were provided from each load lot and feedlot so a prevalence rate of TTNS could not be calculated.

Variables included feedlot identification, lot identification, percentage of TTNS in each lot, percentage of population by source, and percentage of TTNS by source. Lots with only single sourced cattle were included in the analysis; multiple sourced lots were excluded.

The database was organized in Microsoft Excel (Microsoft Office, v.15, Microsoft Corporation, Redmond, WA, USA). All descriptive statistics were calculated using Microsoft Excel.

3.3 RESULTS

3.3.1 CASE SERIES

The electronic database included retrospective data on 702 confirmed cases of toe tip lesions that were necropsied and is summarized in Table 3.1. The majority of animals, 77.6% (n=545) were derived from auctions, 9.8% (n=69) were back-grounded, 7.5% (n=53) from pasture, 4.1% (n=29) were ranch direct, and 0.9% (n=6) had no sources available.

Of the 702 cases, 55% (n=384) were yearlings and 45% (n=318) were calves. Steers accounted for 71% (n=497) and heifers accounted for 29% (n=205) of necropsied cases.

There were 30% (210/702) of necropsied cases treated for TTNS and 70% (492/702) that were not treated. Of those animals treated, the mean and standard deviation (median) interval from feedlot arrival to first treatment was 18.9 ± 1.7 d (12 d). The mean (and standard deviation) days from arrival to first treatment for TTNS for auction derived animals was 20.4 ± 27.6 d, grass derived was 13.6 ± 8.3 d, background was 17.4 ± 18.9 d, and ranch direct at 16.2 ± 5.0 d ($P = 0.53$). There was no difference in time of first treatment for TTNS based on calves (20.8 ± 29.7 d) or yearlings (17.53 ± 19.5 d) ($P = 0.34$); also there was no difference in time of first treatment for TTNS in steers (18.8 ± 25.2 d) or heifers (19.1 ± 22.2 d) ($P = 0.94$). There was no difference in the mean days on feed until first treatment for TTNS in each year (2008-2012) ($P = 0.13$).

There were 75.2% (528/702) TTNS cases euthanized. Based on the 702 cases the mean (median) interval from feedlot arrival to death was 42.7 ± 1.7 d (27.0 d). The mean (standard deviation) days on feed until death from TTNS were the earliest in grass-fed calves (32.4 ± 22.1 d), auction-derived (40.6 ± 40.6 d), ranch direct (44.1 ± 53.1 d), and then back-grounded calves (69.0 ± 75.6 d) ($P < 0.001$). Yearlings were only on feed for mean (standard deviation) days of 37.1 ± 32.0 d when compared to calves at 49.5 ± 57.0 d before death ($P < 0.001$). There was no difference in time of death between steers and heifers ($P = 0.23$). Collectively, Figure 3.1 shows an epidemic curve that illustrates the frequency distribution of the number of days on feed until first treatment for TTNS and number of days on feed until death.

There was no difference in the annual mean (standard deviation) days on feed until first treatment for TTNS over the five years: 2008 (13.0 ± 8.7 d), 2009 (25.3 ± 36.4 d), 2010 (16.4 ± 14.1 d), 2011 (19.0 ± 25.2 d), and 2012 (17.9 ± 22.5 d) ($P = 0.13$). There was a difference in the

annual mean (standard deviation) days on feed until death over the five years: 2008 (31.0 ± 25.4 d), 2009 (42.6 ± 40.7 d), 2010 (42.9 ± 40.9 d), 2011 (46.6 ± 50.7 d), and 2012 (85.1 ± 92.8 d) ($P < 0.001$).

Table 3.2 illustrates the monthly distribution of deaths associated with TTNS. The greatest proportion of deaths occurred from September to November.

3.3.2 LOT PREVALENCE

The lot-level prevalence of toe tip lesions was based on 1,904 separate lots in 48 feedlots during January 1 to December 31, 2012. The lots represented a total of 616,831 feedlot animals. Lot sizes ranged from 100-5,443 cattle.

Figure 3.2 shows the prevalence of TTNS within a lot of feedlots that have greater than one case of necropsied TTNS per lot. The majority of lots (1,832/1,904) did not have any cases of TTNS at necropsy when compared to 54/1,904 lots that had a TTNS prevalence of 0.01-0.30%.

Figure 3.3 illustrates the percent of lots within the 48 feedlots that had >1 necropsy case of TTNS. Feedlot 23 and 25 had a greater percentage of TTNS in each lot when compared to feedlot 18 and 19.

3.4 DISCUSSION

Based on 702 necropsied TTNS cases the data shows that this condition develops early in the feeding period. The arrival to first treatment interval suggests that either animals enter the feedlot with TTNS, or develop the condition during initial feedlot handling. Since the distribution of cases may be related to transport or initial handling or both, TTNS could be referred to as a transport or arrival related disease.

With reference to Table 3.1, the year 2007 will be ignored in the interpretation of results. As seen there were only two cases recorded in that year compared to the following years (2008-

2012, inclusive). Upon further investigation as to why there was such an increase in cases seen during subsequent years, 2007 was a year in which there were significant changes to the computerized record-keeping software. A database prior to 2007 was in the process of being eliminated and a new database was being installed. Therefore, some feedlots only had cases archived in the database for 2007 that is seen in Table 3.1. This type of information bias needs to be considered in further interpretation.

The majority of cattle with TTNS were derived from an auction source (545/702) followed by background-derived (69/702), and grass sourced (53/702). This demographic of sources changes from year to year as the Canadian-US dollar exchange, feed availability, and international export requirements all impact where cattle are purchased. By source, there was no difference in the arrival to first treatment of TTNS and is likely explained that only 30% (210/702) of animals were treated that reduced the sample size. However, there was a difference in days on feed until death by source of animals. Grass-fed and auction derived animal died earlier from TTNS than did ranch-direct and background animals. If the mechanical trauma theory is correct in TTNS pathogenesis this could have an impact on the quality of horn, or the degree of damage sustained by the claw. For example, grass fed cattle may have softer horn in the claw that predisposes to injury. Auction-derived cattle also spend more time on hard, abrasive, and concrete surfaces during transportation and processing times at the feedlot. Both of these scenarios could contribute to disruption of claw integrity. Collectively, the greater the damage to the claw and impact on the lesion will allow the disease to progress quicker.

There appeared to be more steers (501/702) than heifers (201/702) that are affected by this condition but there is no denominator for comparisons to be drawn. However, there was no difference in gender (steer, heifer) in treatment times or days on feed until death for TTNS.

In western Canada, the fall months (September, October, and November) are referred to as "fall run" meaning cattle entry into the feedlot is at a peak. Over the past five years (2011-2014) feedlot placements are highest in September, October, and November. Roughly 290,000 head of cattle will enter feedlots in Alberta and Saskatchewan when compared to approximately 65,000 head of cattle that enter feedlots in June and July (CanFax, 2014). As depicted in Table 3.2, deaths due to TTNS occur in all months of the year; however, September, October, November, and December have the greatest percentage (67.9%; 477/702) of TTNS deaths. Not surprisingly, TTNS deaths would be expected to increase as the total population of cattle that enter the feedlot increases. Therefore, the month of year is speculated to be a confounding factor for TTNS occurrence as its dependent on the total cattle that enter the feedlot.

TTNS affects calves (318/702) and yearlings (384/702). This is an interesting observation as some practitioner's commented that only calves were afflicted by toe tip lesions. There is no difference in treatment times between ages, but this study found that yearlings died earlier than calves from TTNS. It is hypothesized that since yearlings, as a general rule, are heavier than calves that the disease in the foot will negatively affect their production at a faster rate. The fluctuation in the percentage of calves and yearlings with TTNS over the years 2008-2012 most likely reflects the demographics of purchased cattle which suggest that age is also a confounding variable.

The epidemic curve highlights that TTNS occurs soon after feedlot arrival. Since treatment for TTNS occurs on day one after arrival to the feedlot it suggests that animals may come to the feedlot with this condition. It is likely that, based on the mechanical trauma theory, facility design at the animal's origin is just as able to cause damage to the claw as is the trailer used for transportation. From the epidemic curve there are TTNS cases that are dying later into

the feeding period. This observation could be due to the treatment crew that decides when an animal should be euthanized as there does not appear to be another point source, such as re-implanting, that causes a sudden increase in cases.

The median days on feed at first treatment for TTNS were consistent throughout the five years (2008-2012). The median days on feed at first treatment reflects the reliability and attentiveness of pen riders and treatment crews when identifying animals with clinical signs of lameness. Interestingly, this period of time after feedlot arrival did not vary from year to year despite always having different populations of animals enter the feedlot. Notably, the median days on feed at first treatment provide an objective measurement that TTNS is an arrival or transport-related condition.

As shown in Figure 3.2 there were 96.2% (1,832/1,904) of lots without one case of TTNS. Conversely, there were 3.8% (72/1,904) of lots with one or more TTNS cases. Another salient feature is that TTNS cases can cluster together. In addition, Figure 3.3 shows that TTNS can also cluster at the feedlot level. For example, feedlot 23 and 25 had $\geq 50\%$ lots affected by at least one case of TTNS whereas other feedlots (2, 5, 6, and 9 for example) did not have any cases within lots. The clustering effect of TTNS cases supports practitioner's anecdotal experiences of groups of cattle being at a greater risk than other groups. Often animals are handled in a similar method, for example, groups of cattle are exposed to the same environmental conditions, facility design, transported, and enter the feedlot at the same time. In addition to the direct effects of flooring on the claw there are also indirect effects, such as nutrition and behavior that could predispose animals to claw lesions. Practitioners suggest there is a greater prevalence of TTNS in hyper-excitable cattle. It is hypothesized that hyper-excitable animals have a predisposition to avoid human contact, and as such, animals will make quick movements and sudden turns to

avoid that human encounter which allows for greater pressure on certain areas of the claw.

Nutrition and the role of micronutrients should also be studied in greater detail as the structure and function of the claw depends on the optimal level of micronutrients present.

The lack of total populations, including those animals that did not succumb to TTNS, for the retrospective and prevalence database was a major limitation in this study. Without a denominator there is an inability to determine the risk of TTNS for incoming cattle. Also the retrospective database and lot-level database did not span the same number of years. To avoid ecological fallacy one must carefully differentiate the descriptive database separate from the lot-level database. To make inferences from a population database to the individual animal is a bias. There was subjectivity present in classification of ages in the descriptive database as different feedlot personnel were tasked with record keeping.

Despite previous case descriptions of TTNS this is the first descriptive epidemiological study in western Canadian feedlot cattle. This study showed that TTNS is a transport or arrival related condition and has a propensity to cluster. Future work should focus on identification of risk factors and causal relationships for TTNS occurrence.

Table 3.1: Retrospective summary of 702 cases of Toe Tip Necrosis Syndrome for the years 2007-2012, inclusive.

Variable	Year						Total
	2007	2008	2009	2010	2011	2012	
Source							
Auction	100.0%(2/2)	88.8%(183/206)	84.9%(180/212)	70.3%(109/155)	58.7%(57/97)	46.6%(14/30)	77.6%(545/702)
Rauch	0.0%(0/2)	0.5%(1/206)	8.5%(18/212)	2.6%(4/155)	5.1%(5/97)	3.3%(1/30)	4.1%(29/702)
Background	0.0%(0/2)	5.8%(12/206)	3.3%(7/212)	10.9%(17/155)	21.6%(21/97)	40.0%(12/30)	9.8%(69/702)
Grass	0.0%(0/2)	4.9%(10/206)	3.3%(7/212)	15.4%(24/155)	11.3%(11/97)	3.3%(1/30)	7.5%(53/702)
Unknown	0.0%(0/2)	0.0%(0/206)	0.0%(0/212)	0.6%(1/155)	3.0%(3/97)	6.6%(2/30)	0.8%(6/702)
Age Class							
Calves	100.0%(2/2)	26.6%(55/206)	70.7%(150/212)	36.7%(57/155)	48.4%(47/97)	23.3%(7/30)	45.2%(318/702)
Yearlings	0.0%(0/2)	73.3%(151/206)	29.2%(62/212)	63.2%(98/155)	51.5%(50/97)	76.6%(23/30)	54.7%(384/702)
Gender							
Steer	50.0%(1/2)	68.9%(142/206)	66.9%(142/212)	70.3%(109/155)	76.2%(74/97)	73.3%(22/30)	71.3%(501/702)
Heifer	50.0%(1/2)	31.0%(64/206)	33.0%(70/212)	20.6%(32/155)	23.7%(23/97)	26.6%(8/30)	28.6%(201/702)
Euthanized							
Yes	50.0%(1/2)	69.4%(143/206)	78.1%(161/206)	86.4%(134/155)	68.0%(66/97)	76.6%(23/30)	75.2%(528/702)
No	50.0%(1/2)	30.5%(63/206)	24.8%(51/206)	13.5%(21/155)	31.9%(31/97)	23.3%(7/30)	24.7%(174/702)
MDOFT ¹ (days)	N/A	11.5	13.0	12.0	13.0	11.5	12.0
MDOFD ² (days)	165.0	26.0	26.0	30.0	26.0	21.0	26.0
MAW ³ (lbs)	597.5	774.5	617.0	755.5	710.5	789.0	733.0
MFMW ⁴ (lbs)	626.0	700.0	599.5	700.0	700.0	750.0	700.0

¹Median Days on Feed At First Treatment

²Median Days on Feed At Death

³Median Arrival Weight

⁴Median Post Mortem Weight

Table 3.2: Proportion of Toe Tip Necrosis Syndrome Deaths Each Month from 2007-2012.

Month	Number of Deaths	Proportion
January	35	0.05
February	31	0.04
March	15	0.02
April	30	0.04
May	28	0.04
June	27	0.04
July	35	0.05
August	24	0.03
September	118	0.17
October	123	0.18
November	154	0.22
December	82	0.12
<i>Total</i>	702	1.00

Table 3.3: Proportion of Lots with Toe Tip Necrosis Syndrome (TTNS) in 48 Western Canadian Feedlots, January 1, 2012 to December 31, 2012.

Source	TTNS Status			
	Positive		Negative	
	Proportion	Frequency	Proportion	Frequency
Auction	0.04	(30/765)	0.96	(735/765)
Ranch Direct	0.01	(2/149)	0.99	(147/149)
Grass	0.02	(3/198)	0.98	(195/198)
Background	0.03	(10/390)	0.97	(380/390)
Average	0.03	(45/1502)	0.97	(1457/1502)

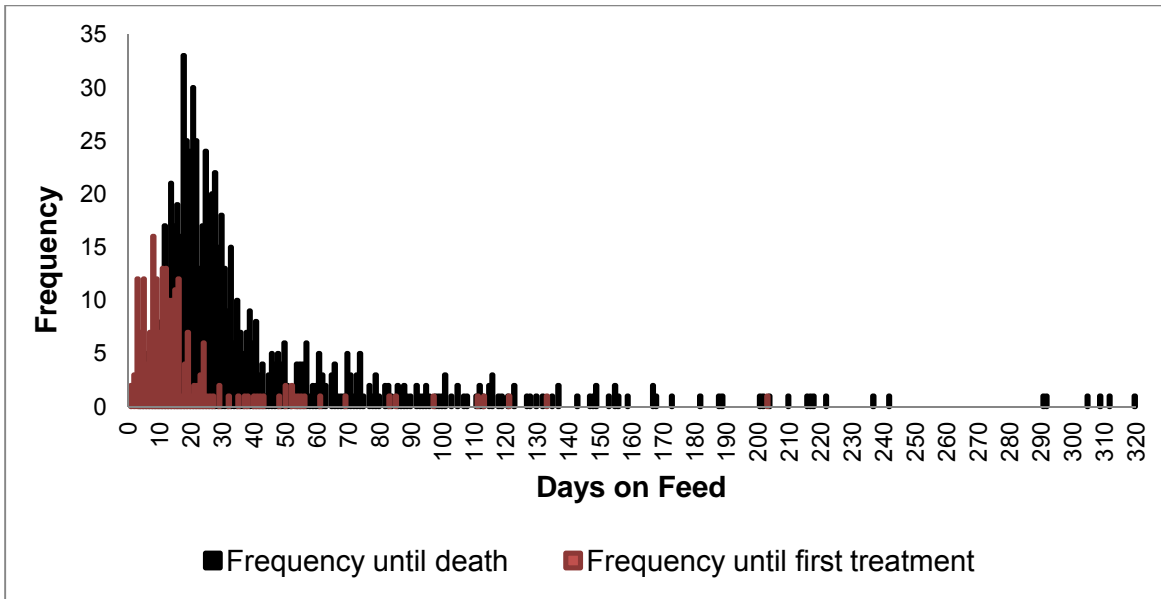


Figure 3.1: Frequency distribution of the number of days on feed until first treatment for TTNS (n = 210) and number of days on feed until death (n = 702).

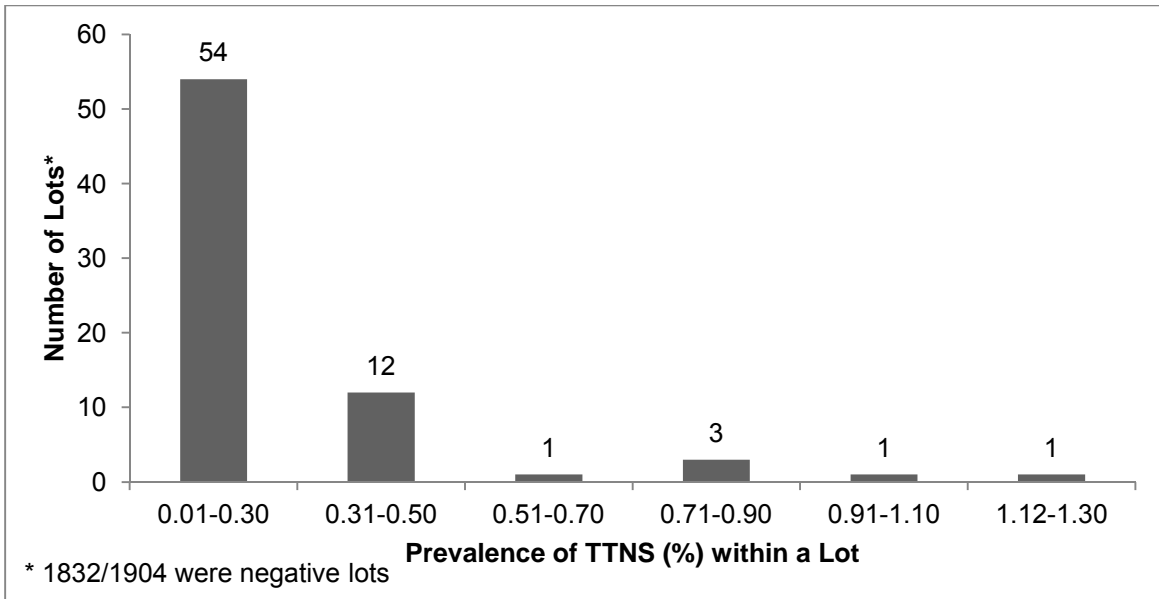


Figure 3.2: Prevalence of Positive Lots (n = 72) for Toe Tip Necrosis Syndrome (TTNS) in a total of 1,904 lots of cattle shipped to 48 separate feedlots for the period January 1 to December 31, 2012.

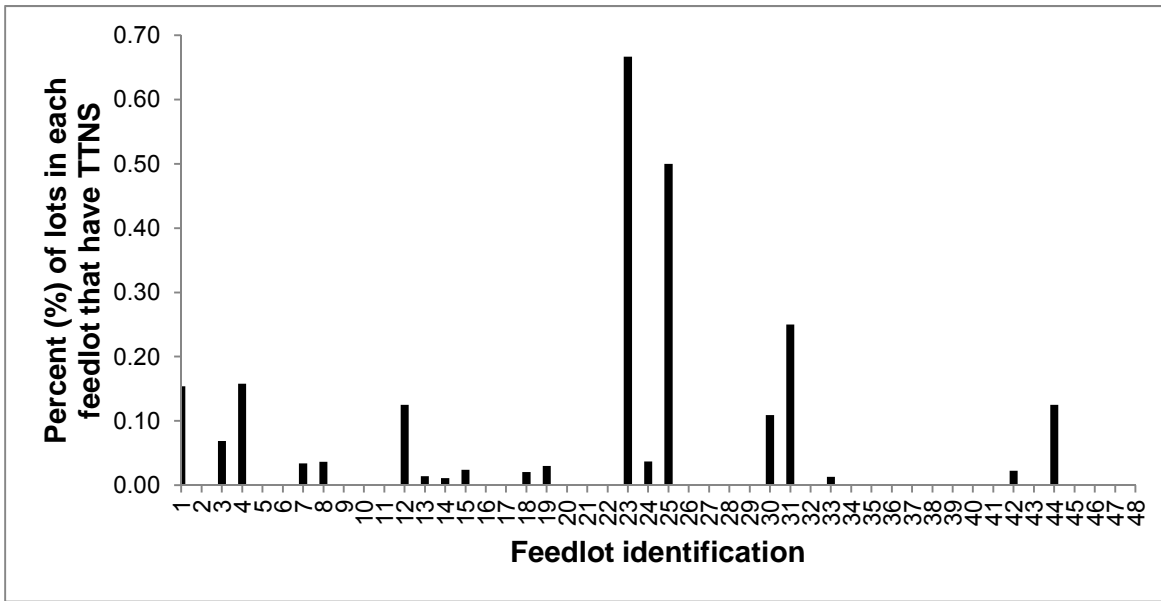


Figure 3.3: Percent (%) of lots within each feedlot operation having at least 1 case of Toe Tip Necrosis Syndrome (TTNS) for the period January 1 to December 31, 2012.

CHAPTER 4: PROSPECTIVE CASE CONTROL STUDY OF TOE TIP NECROSIS SYNDROME IN WESTERN CANADIAN FEEDLOT CATTLE

4.1 INTRODUCTION

Toe tip lesions have been described in the literature (Sick *et al*, 1982; Dewes *et al*, 1979; Miskimins, 1994). Multiple names have been used to describe toe tip lesions, most notably, "toe abscess", "P3 necrosis", "apicus necrotica", "apical pedal bone necrosis", and "toe necrosis". In order to describe toe tip lesions in a thorough and universal manner a new more specific term has been proposed, Toe Tip Necrosis Syndrome (TTNS). TTNS is characterized by a separation of the apical white line of the claw with tissue necrosis and clinical lameness. This term encompasses complications such as pedal (P3) osteitis, middle (P2) and proximal (P1) phalangeal osteomyelitis, tenosynovitis, cellulitis, and embolic pneumonia.

Due to a lack of epidemiological studies about TTNS, practitioners' anecdotal experiences are currently used in treatment and prevention of this condition. Anecdotal reports have hypothesized viral, bacterial, nutritional, or behavioural risk factors that contribute to TTNS. Specifically, a greater prevalence of TTNS is suspected in hyper-excitable cattle and bovine viral diarrhea virus (BVDV) involvement has been suggested; however, neither epidemiology nor pathogenesis have been critically evaluated.

There are currently three theories regarding the pathogenesis of TTNS: mechanical trauma to the claw, pedal bone vascular disruption, and as a sequela to laminitis. Sick *et al* (1982), Miskimins (1994), and Greenough (2007) hypothesized that toe abscesses, which are descriptively similar to TTNS, result from abrasion, rasping, and trauma to the claw during transportation and processing of feedlot cattle. Not only does facility design and transportation lead to mechanical trauma but iatrogenic causes can lead to claw damage. Thompson (1998) and Kofler (1999) reported that overzealous or incorrect claw trimming can lead to white line separation that manifests as pedal osteitis.

Greenough (2007) has also postulated that toe tip lesions could start from vascular impediments to the pedal bone. During periods of prolonged standing in auction yards or livestock trailers there could be hypostasis of blood in the distal limb. Since the distal extremity relies on the passive movement of blood flow through arteriovenous anastomoses during ambulation, but as the animal stands this process could be impaired. This alteration in microcirculation could devitalize the pedal bone due to a lack of collateral circulation. It has been reported, by the same reference, that when the blood supply to the pedal bone is impaired a thrombus can lead to a fracture of the apical pedal bone. Due to the increased pressure inside the claw as a result of inflammation, ischemia, and necrosis the white line can rupture near the apex of the claw. This theory is suggested as some animals have no visible opening in the claw and therefore the lesion may start internally. Alternatively, there could be a vasculitis process that occurs within the affected animal. A common pathogen that affects feeder cattle known to cause a vasculitis is BVDV (Radostits *et al*, 2007).

A third theory in the pathogenesis of TTNS is a potential sequelae to laminitis. Laminitis, by definition, is an acute degeneration of the laminae of the claw that results in pedal bone rotation (Radostits *et al*, 2007). There are acute, subclinical, and chronic manifestations. In cattle, phalangeal rotation has been seen in acute and chronic laminitis (Andersson and Bergman, 1980). Laminitis can be secondary to ruminal acidosis, which is due to irregular feeding patterns and sudden changes of diets. Since animals that have recently entered a feedlot experience nutritional stress it is hypothesized that the rotation of the pedal bone can damage the corium, which allows for white line breakdown. It has been suggested by Greenough *et al* (1990) that osteopathy of the apex of the pedal bone is more common in calves than yearlings due to dietary changes.

There have been no studies to document the current theories on TTNS pathogenesis. A causal diagram as shown in Figure 4.1 illustrates the hypothesized risk factors for TTNS. The objective of this chapter was to identify potential risk factors for toe-tip necrosis syndrome (TTNS) in western Canadian feedlot cattle.

4.2 MATERIALS AND METHODS

4.2.1 PRACTICE SELECTION

A non-random convenience sampling procedure was used to select veterinary practices to participate in this study. During August 2012, four veterinary practices in Alberta were asked to participate in a case-control study: Feedlot Health Management Services, Okotoks; Veterinary Agri-Health Services, Airdrie; Alberta Beef Health Solutions Inc., Picture Butte; and Coaldale Veterinary Clinic Ltd., Coaldale. A follow-up letter outlined a confirmed case as an animal at necropsy having apical white line separation and pathology consistent with necrosis that involved the distal phalanx. A control animal was the next animal to be necropsied, which could be from a different lot than the case animal but similar in days on feed, weight, and age class that had no apical white line separation or pathology of the distal phalanx. The individual animal records, which accompanied the submitted tissues, included information on the number of days on feed, arrival weight, treatment history, pen identification, lot identification, feedlot identification, and Canadian Cattle Identification Agency (CCIA) tag number. Sample kits contained supplies to be used for tissue collection and a picture booklet that showed apical white line separation in claws.

4.2.2 SAMPLE COLLECTION AND EVALUATION

Participating practices were requested to submit claws sectioned at the level of the mid-metatarsal or metatarsophalangeal joint. In addition, 10% neutral buffered formalin fixed cardiac and skin tissue from both case and control animals were requested. Specifically, a cross-section

of the septum was necessary for the cardiac muscle. Skin samples were obtained from the distal limb and placed in formalin for those limbs that did not have skin tissues submitted. Cardiac muscles were submitted to Prairie Diagnostic Services (PDS; Saskatoon, Sk) for histopathological evidence of vasculitis. Formalin fixed tissues (cardiac, skin) were submitted to PDS be tested by immunohistochemistry for bovine viral diarrhoea virus (BVDV). Laboratory personnel involved in all testing were blinded as to which samples were cases versus controls.

All frozen distal limbs were sagittally sectioned with a band saw to determine if the field veterinarian's diagnosis of a case or control were consistent with the study definition of TTNS. A 1-2 cm thick sagittal section of the medial and lateral claw was obtained from midpoint of the claw parallel to the axial wall. Examination of the distal limb sections confirmed toe tip necrosis syndrome and were recorded. Digital photographs (Nikon CoolPix L810, Nikon Canada, Mississauga, Ontario, Canada) were taken of one sagittal section per claw. An anaerobic and aerobic culture swab (BBL CultureSwab, Becton, Dickinson and Company; Sparks, Maryland, USA) were taken from the sectioned surface of the pedal bone and submitted to Prairie Diagnostic Services (PDS, Saskatoon, Saskatchewan) for bacteriological culture. The swabs were cultured using blood agar and MacConkey's culture plates (Becton, Dickinson and Company; Sparks, Maryland, USA).

4.2.3 BACTERIAL CULTURE

All swabs are cultured on blood and MacConkey agar plates (Becton Dickinson and Company, Sparks, Maryland, USA). One set of blood agar and MacConkey plates were incubated at 37°C, in 5% CO₂ and another set of blood agar plates were incubated anaerobically at 37°C for a maximum of 48 hours. Bacterial cultures were quantified and identified using basic biochemical tests (Quinn *et al*, 1993).

4.2.4 HISTOPATHOLOGY

Tissue samples (cardiac and skin) were fixed in 10% neutral buffered formalin, and routinely processed and embedded in paraffin wax. Sections four micrometers thick were cut from a tissue block and stained with hematoxylin and eosin (HE). The HE sections were examined under light microscopy. Tissue sections were examined for evidence of vasculitis, perivasculitis or periarteritis which included inflammatory cells in a vessel wall, necrosis of smooth muscle, or thrombosis inside a vessel. The remaining sections from each tissue block were processed for immunohistochemistry.

4.2.5 IMMUNOHISTOCHEMISTRY

Immunohistochemical staining for bovine viral diarrhea virus was conducted using a commercial staining platform (Benchmark staining platform, Ventana Medical Systems, Tuscon, AZ) and an HRP-labeled multimer detection system (BMK Ultraview DAB Paraffin detection kit, Ventana Medical Systems, Tuscon, AZ). Enzymatic epitope retrieval was performed (Protease 3, Ventana Medical Systems, Tuscon, AZ) and the primary antibody (Mouse anti-BVD clone 15c5) was applied for 32 minutes at a dilution of 1:500 (Haines *et al.*, 2004).

4.2.6 CLAW MEASUREMENTS

Digital photographs were uploaded into an imaging processing software (Fiji, Continuous release version). Claw characteristics were electronically measured on the sagittal sections in the imaging software. Prior to measurements, the imaging program was calibrated using a millimeter scale within the image. As seen in Figure 4.2, dorsal thickness "A" was the thickness of the dorsal hoof capsule at the midpoint between the periople and apex of claw. Dorsal thickness "B" was the thickness of the dorsal hoof wall capsule at the corium. Sole thickness "C" was the thickness of the sole at the white line. Sole thickness "D" was the thickness of the sole at the ventral contour of the pedal bone. Sole thickness "E" was the thickness of the sole at the plantar

aspect of the pedal bone. Angle measurements were taken of the claw capsule and the pedal bone. Angle "A" was the outer dorsal hoof wall and sole. Angle "B" was the inner dorsal hoof wall and sole. Angle "C" was the dorsal aspect of pedal bone and sole. Angle "D" was the dorsal and ventral pedal bone.

4.2.7 SAMPLE SIZE CALCULATION

Sample size was calculated for a case control study, 98 samples would have been necessary for each group (total sample size of 196) to measure an expected proportion of 0.05 in control animals with 95% confidence level, 80% power and an assumed odd's ratio of 4. (EpiTools Epidemiological Calculators, 2014; Queensland, Australia).

4.2.8 DATA ANALYSIS

Data was manually entered into a database (Microsoft Access v. 14; Microsoft Corporation, Redmond, Washington, USA). All descriptive statistics were calculated using a commercial spreadsheet program (Microsoft Excel v. 12; Microsoft Corporation). The database was then transferred to a statistical program, SPSS (Version 20, SPSS Inc., Chicago, IL, USA) for analysis. The *P-value* was set at 0.05.

Confirmation of toe tip lesions in the feet was compared to the field diagnosis of TTNS classification (case/control). A 2 x 2 table was used to determine the kappa statistic, positive predictive value (PPV), and negative predictive value (NPV). Microbiological culture results from the pedal bone were recorded as quantified by the laboratory. Histopathological vasculitis results and immunohistochemistry (IHC) results of bovine viral diarrhoea virus were reported as dichotomous variables. Chi-square analysis was used to compare the frequency of BVDV and vasculitis lesions to TTNS classification. Fisher's Exact test was used to compare the frequency of tissue IHC results with TTNS classification. Dorsal hoof wall, sole thickness, and angle measurements were reported as continuous variables. Two-sample t tests were used to compare

the measurements between TTNS classification. Statistical assumptions were met prior to testing: normal distribution, simple random sample, independence, expected frequencies in cross tabulation table are all greater or equal to five (Chi-Square) or less than five (Fisher's Exact).

Exclusion criteria of cases and controls were missing health records, misplaced feet, absent cardiac tissue, or digital images where the sole was absent. This lack of information could not confirm a toe tip lesion, laboratory findings, or solar measurements and could have resulted in misclassification of cases versus controls.

A previous equine laminitis study found an objective evaluation of pedal bone rotation was to determine the difference between the dorsal hoof angle relative to the ground surface and the dorsal pedal bone angle relative to the ground surface (Sloet van Oldruitenborgh Oosterbaan, 1999). This method was attempted for determination of bovine laminitis in this study.

4.3 RESULTS

Frozen and formalin fixed tissues were collected from three practices and sent to the Western College of Veterinary Medicine (WCVM) by a commercial courier service (Purolator Inc., Mississauga, Ontario, Canada). Frozen samples were stored in a -20°C freezer until examined. During the collection period of October 2012 to January 2013, inclusive, there were a total of 148 submissions that consisted of 82 cases and 66 controls from 16 different feedlots.

Confirmation of case and control classification at the Western College of Veterinary Medicine was based on gross examination and digital images from sagittal sections. A total of 135 animals were in the database, 67 cases and 68 controls. There were 13 missing samples. The measure of agreement (kappa) between the veterinary practice and the diagnosis of TTNS, as confirmed after cut using the band saw at the WCVM, was 0.778 ($P < 0.001$). The positive (PPV) and negative predictive values (NPV) were 0.84 (64/76) and 0.95 (56/59), respectively.

The microbiological culture results showed that 75% of pure isolates (greater than five colonies per quadrant) were attributed to *Escherichia coli*, *Streptococcus* spp., *Trueperella pyogenes*, *Fusobacterium necrophorum* in TTNS cases. The remainder of isolates consisted of *Pseudomonas aureginosa*, *Corynebacterium* spp., *Enterobacter* spp., *Proteus* spp., and *Staphylococcus* spp.. Of the TTNS control animals, 61% of pure isolates consisted of *Enterobacter* spp., *Corynebacterium* spp., and *Streptococcus* spp.; the remainder included *Escherichia coli*, *Trueperella pyogenes*, *Fusobacterium necrophorum*, *Pseudomonas aureginosa*, and *Staphylococcus* spp.

Table 4.1 is a contingency table of the number of TTNS case and control animals, and the frequency of BVDV (cardiac muscle, skin) and vasculitis (cardiac muscle). Bovine Viral Diarrhea virus was found in TTNS case and control animals; however, TTNS animals were 3.8 times more likely than control animals to have BVDV isolated (95% CI: 1.7-8.5; $P < 0.001$). In addition, TTNS animals were 2.2 times more likely than control animals to show histopathological evidence of vasculitis (95% CI: 1.0-4.6; $P = 0.04$). BVDV samples were 11.2 times more likely to have histopathological evidence of vasculitis than non-BVDV samples (95% CI: 4.7-27.0; $P < 0.001$). There was no association between BVDV antigen location in tissues and case animals ($P = 0.55$)

Based on 66 TTNS case animals the mean \pm standard deviation (median) days on feed until death was 26.74 ± 11.90 (26.00) days. Sixty four TTNS control animals had a mean \pm standard deviation (median) days on feed until death of 33.02 ± 16.92 (32.00) days.

Table 4.2 contains descriptive statistics on claw biometrics that were measured between TTNS case and control animals. Table 4.3 shows there was no differences in claw thicknesses of the dorsal wall, nor were there any differences in angles. A difference was found in sole

thickness at site "C" ($P < 0.001$). However, sole thickness at site "D" or site "E" were not significant.

The difference between the dorsal hoof wall angle relative to the sole (Angle A) and the dorsal pedal bone relative to the sole (Angle C) was found to not show any significant pedal bone rotation ($P = 0.15$).

4.4 DISCUSSION

This study demonstrated an association of bovine viral diarrhea virus, vasculitis, and apical sole thickness with TTNS. These risk factors as determined by a prospective case control study do not imply causation just association. Nonetheless, it is speculated that the above-mentioned risk factors can relate to mechanical trauma of the claw as a potential theory for TTNS pathogenesis.

In reference to the mechanical trauma hypothesis, as animals are transported from the farm of origin to the feedlot there are different types of flooring that these animals will stand on. The ground at pasture or within a corral is relatively soft and absorbs an animal's weight. When the same animal is placed on a livestock trailer, auction mart or within a processing chute there is a sudden change in the composition of flooring that includes iron grates, concrete flooring, and/or slatted floors. The change in facility design coupled with sudden turning, quick and lunging movements, places mechanical stress on the weight-bearing claws. Van der Tol *et al* (2002) reported the lateral claw bears more weight than the medial claw on the hindlimb; therefore, another hypothesis would be that more stress-related changes would be seen in the lateral claw in TTNS cases.

As a result of abrasion, rasping, and shearing-type motions, the claw would be expected to be thin or damaged. Based on this study, the apical sole thickness (site C) was found to be decreased in TTNS cases when compared to controls. Interestingly, the sole thickness at site D

was found to also be decreased between the two groups; however, it was not statistically significant ($P=0.06$). This trend towards significance may have become statistically significant given a greater sample size. Regardless of the thickness of the dorsal wall of the claw the apical sole thickness is a risk factor for TTNS occurrence.

Due to a thin apical sole it is hypothesized that the claw integrity will be reduced that would allow in separation of the dorsal wall and sole at the apical white line. In theory, this breach in the claw capsule could likely become a portal of entry into the foot. This non-union in the wall and sole acts as a “hinge” which opens and closes when the animal walks. During movement, fecal material, present in the environment, is collected in the apex of the claw. This is supported by the environmental pathogens that were aerobically and anaerobically cultured from the pedal bone in TTNS cases. *Escherichia coli* and *Fusobacterium necrophorum* are pathogens that are commonly found in fecal material of the feedlot environment. *Trueperella pyogenes* is a bacterium frequently isolated from any purulent inflammatory process, which would include a pedal osteitis. In contrast to the control animals where *Enterobacter* spp., *Corynebacterium* spp., and *Streptococcus* spp were found; these bacteria would be explained as normal commensal micro-organisms. The culture results yielded a mixed population of bacteria in this study. The pure culture on the pedal bone would suggest that the presence of those pathogens would be significant in the pathological process. Smith and Brodersen (1998) were able to isolate *Mycoplasma* spp., in addition to *Bacteroides* spp. and *Fusobacterium* spp., from joint cultures in acutely lame cattle that entered the feedlot. Since *Mycoplasma* spp. can cause polyarthritis in recently arrived feedlot cattle it would make sense to isolate this bacterium from affected joints, but that study did not specify the pedal bone.

This was the first study to report an association between BVDV and TTNS. This finding supported anecdotal evidence from practitioners, but the role of BVDV is still unknown. The virus is known to cause a vasculitis. Therefore, reduced blood perfusion and a decreased integrity of the vasculature in the foot could allow for corium disruption. The breakdown in the barrier of the corium could allow the environmental pathogens to transverse the corium that results in pedal osteitis rather than white line disease, which is contained below the corium. In addition, BVDV is known to cause immune suppression (Radostits *et al*, 2007). Thus the bacterial populations have the ability to and spread more rapidly, which may exacerbate the disease.

With reference to Table 4.1, there were 43.1 % of cases that had BVDV isolated when compared to 16.7% of control animals. One suggested explanation could be that chronically lame animals are more likely to be removed from their home pen and placed in a hospital pen. By nature, the hospital pens contain other animals with respiratory, gastrointestinal and musculoskeletal ailments. It is likely that chronically sick animals can harbor BVDV and transmit the virus during their stay in the hospital pen. Therefore, despite animals that have a chronic lameness the BVDV infection could have resulted from the recent transmission from infected pen mates and could be a secondary finding. Or the transmission of BVDV while the lame animal is in the hospital pen could suppress the animal's immune system and allow for a rapid decline in the primary TTNS condition. Or there could be a persistently infected BVDV animal in a lot of cattle that may contribute to the development of TTNS lesions. What is missing is the time sequence or temporality. Temporality is a criterion that indicates the effect (TTNS) occurs after the cause (BVDV) and is used to provide adequate evidence of causation (Dohoo *et al.*, 2009). The BVDV findings in this study do not provide any indication to temporality, and as such, should be further investigated in experimental studies.

The findings of this study also show that vasculitis was associated with TTNS. Importantly, BVDV and vasculitis are significantly associated to each other. Therefore, the presence of BVDV is likely contributing to vasculitis lesions. Knottenbelt (2002) and Jayne (2009) report in equine and humans, respectively, other causes of vasculitis would include antimicrobial therapy, bacterial infections, or immunogenic stimulation from vaccinations. In feedlot cattle, these causes could be plausible contributing factors in the early feeding period. BVDV transient vasculitis is not uncommon in feedlot cattle and has been reported to occur in *Mannheimia haemolytica* pneumonia and *Mycoplasma bovis* chronic pneumonia and polyarthritis syndrome. (Dr. Ted Clark, personal communication, September 2013).

There was no difference in the angles measured with respect to the pedal bone on sagittal sections. This was important as laminitis was one of the three current theories on TTNS pathogenesis. Since no rotation of the pedal bone was noted it is unlikely that laminitis was a contributing factor for TTNS.

Examination of the claw in the field based on apical white line separation and tissue necrosis had excellent agreement with WCVM confirmation of sagittal sections. Landis and Koch (1977) suggests that a kappa greater than 0.750 is excellent agreement. This suggests that clinical examination of the claw that shows apical white line separation and tissue necrosis would be suggestive of TTNS. In addition, field diagnosis of TTNS at necropsy can be based on examination, and the practitioner can be confident with a diagnosis. The PPV of 0.84 suggests that 84% of feet diagnosed as TTNS were true cases of TTNS. However, 16% (100% - 84%) of cases were false positives, which suggests that veterinarians were more likely to over diagnose TTNS than to under diagnose at the time of necropsy examination. One possibility is that an early case may have apical white line separation but have no evidence of tissue necrosis. Or

secondly, predictive values are influenced by the prevalence of disease in a population; therefore, the lower PPV could be related to the low prevalence of TTNS. In comparison to the NPV of 0.95 shows that 95% of feet not classified as TTNS were in fact control (non-TTNS) feet. Therefore, the presence of apical white line separation is highly suggestive in a field situation of a TTNS diagnosis.

Potential limitations to this study include misclassification bias in the database due to errors in transcription or recording. The lack of disinfection of the band saw blade during sectioning the feet could contribute to contamination of bacterial culture. Angles measured from the sagittal section could be dependent on the plane of sectioning, but since each section was taken at the midpoint of each claw it reduced the potential for different sections to be compared.

Further studies to investigate the role of vasculitis could be obtained by angiographic evaluation. Future cohort studies of clinical control trials to see if BVDV is causal in TTNS would be indicated. Lastly, field visits to feedlots to classify or rank the environmental conditions and facility design with respect to transport and processing areas would suggest the degree of mechanical trauma to the animal's feet.

The risk factors found in this study can support the findings of anecdotal experiences of practitioners when dealing with TTNS. Bovine viral diarrhea virus, vasculitis, and apical sole thinning are associated with TTNS and should be considered when implementing preventative and treatment strategies. The role of BVDV and vasculitis are still uncertain in disease development, but apical sole thinning supports the mechanical trauma theory to the foot. Practitioners can be assured that field diagnosis of TTNS is accurate on apical white line separation and tissue necrosis, and the pure isolates of bacteria recovered also provide understanding for the pathogens responsible for this disease syndrome.

Table 4.1: Frequency of BVDV, immunohistochemistry location of BVDV antigen, and vasculitis by TTNS case and control animals (n = 131).

Variable	Factor	Case n (%)	Control n (%)	OR	95% CI		<i>P</i> <i>value</i>
					Lower	Upper	
BVDV	Positive	28 (43.1)	11 (16.7)	3.8	1.7	8.5	<0.001
	Negative	37 (56.9)	55 (83.3)	---	---	---	---
IHC*	Cardiac/Skin	4 (14.3)	2 (18.2)	1.3	0.2	8.9	0.55
	Cardiac	24 (85.7)	9 (81.8)	---	---	---	---
Vasculitis	Positive	28 (43.1)	17 (25.8)	2.2	1.0	4.6	0.04
	Negative	37 (56.9)	49 (74.2)	---	---	---	---

* Immunohistochemistry to isolate BVDV antigen.

Table 4.2: Claw characteristics between TTNS case and control animals (n = 127).

Variables	Mean	Median	Standard deviation	Maximum	Minimum
Case					
Dorsal wall (mm)					
Site A (n=64)	4.65	4.60	1.12	8.20	2.56
Site B (n=62)	5.04	5.24	1.32	8.71	2.50
Sole wall (mm)					
Site C (n=64)	3.74	3.66	1.14	7.42	1.14
Site D (n=63)	3.44	3.28	0.78	5.69	2.11
Site E (n=63)	5.71	5.71	1.22	8.65	3.65
Angle (°)					
A (n=64)	56.86	56.43	4.75	68.83	44.39
B (n=64)	58.26	57.54	5.03	69.97	43.77
C (n=63)	58.20	58.54	5.99	72.92	39.76
D (n=63)	52.10	51.71	6.46	69.96	36.77
Control					
Dorsal wall (mm)					
Site A (n=63)	4.75	4.69	0.93	6.79	2.50
Site B (n=61)	5.27	5.22	1.26	8.79	2.84
Sole wall (mm)					
Site C (n=60)	4.72	4.77	1.25	8.05	1.91
Site D (n=62)	3.78	3.47	1.22	8.13	2.04
Site E (n=62)	5.64	5.60	1.32	9.37	3.29
Angle (°)					
A (n=62)	58.12	57.83	5.19	72.45	47.83
B (n=62)	58.78	57.74	4.87	71.46	49.62
C (n=62)	58.35	57.48	4.90	69.38	48.09
D (n=63)	53.68	53.21	4.74	64.50	43.09

Table 4.3: Comparison of mean claw characteristics between TTNS case and control animals (n = 127).

Variable	Case	Control	<i>P-value</i>
Dorsal wall (mm)			
Site A	4.65	4.75	0.62
Site B	5.04	5.27	0.31
Sole wall (mm)			
Site C	3.74	4.72	<0.001
Site D	3.44	3.78	0.06
Site E	5.71	5.64	0.76
Angle (°)			
A	56.86	58.12	0.14
B	58.26	58.78	0.54
C	58.20	58.35	0.88
D	52.10	53.68	0.10

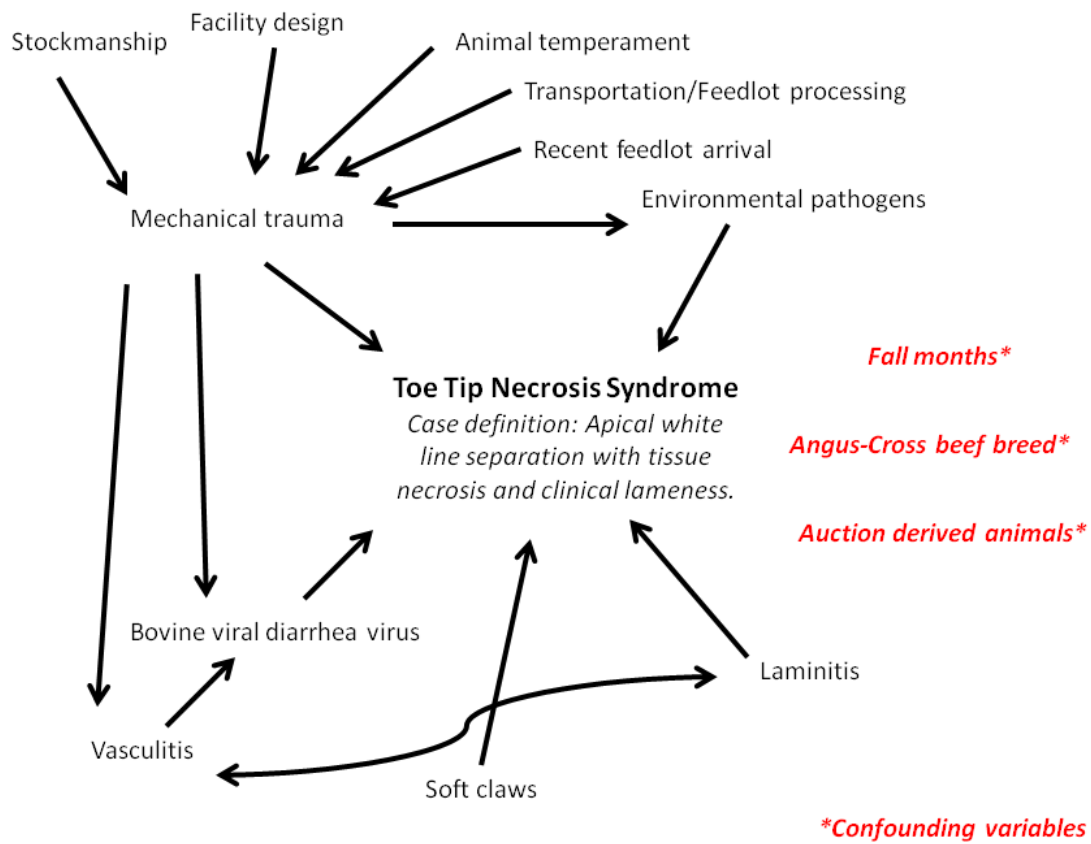


Figure 4.1: Web of causation for TTNS in Feedlot Animals.

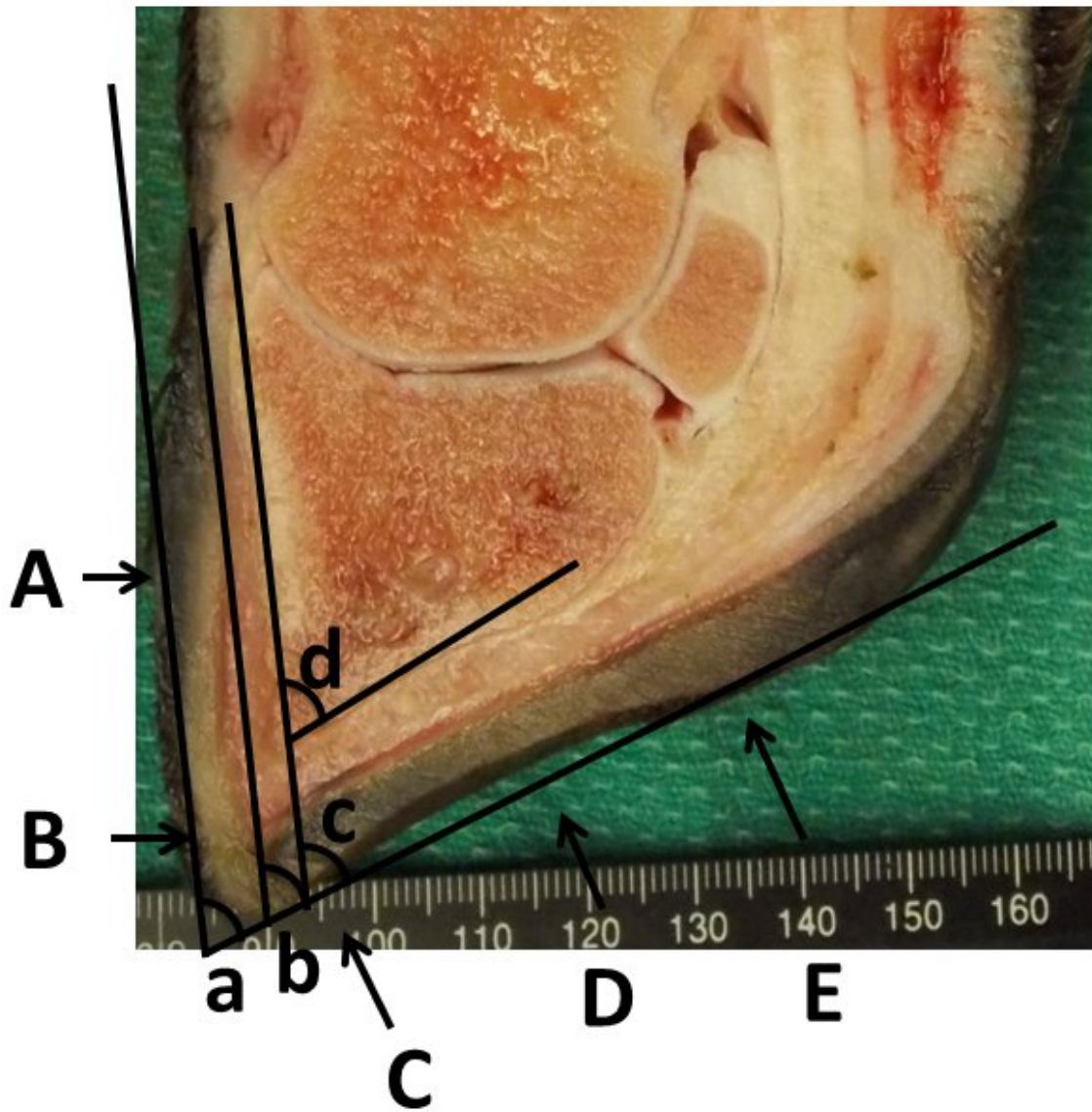


Figure 4.2: Location of claw measurements.

A = thickness of dorsal hoof capsule at midpoint between periople and apex, B = thickness of dorsal hoof wall capsule at solar corium, C = thickness of sole at the white line, D = thickness of sole at ventral contour of pedal bone, E = thickness of sole at plantar aspect of pedal bone, a = angle of outer dorsal hoof wall and sole, b = angle of inner dorsal hoof wall and sole, c = angle of dorsal aspect of pedal bone and sole, d = angle of dorsal and ventral pedal bone.

CHAPTER 5: GENERAL DISCUSSION AND FUTURE RESEARCH

5.1 CONCLUSION

The overall objectives of this thesis were 1) to use clinical examinations, imaging modalities, and necropsy findings to aid in description, classification, and characterization of TTNS lesions, 2) to describe the epidemiology of TTNS in feedlot cattle, and 3) to evaluate risk factors for TTNS. After a thorough literature review and speaking to veterinary practitioners it was evident that there was not a specific, uniform or universal case definition or name for this particular condition.

Chapter 1 introduced a case definition and name that described these lesions. *Toe tip necrosis syndrome* is apical white line separation with tissue necrosis and clinical lameness. The exact location (apical white line), findings (tissue necrosis), and characteristics (clinical lameness) of this disease are very specific. It is hoped that there is universal acceptance of this name and it becomes a commonplace in the vocabulary of practitioners, researchers, and educators in the veterinary community.

Chapter 2 described the epidemiology of TTNS in western Canadian feedlot cattle. The retrospective database used, which was the foundation of this chapter, has not ever been described before in the literature. From these results, there are many important epidemiological features that were identified. For example, the epidemic curve illustrated that TTNS is a transport or arrival-related condition. There was evidence of disease clustering in similar groups of cattle. There appeared to be no gender or age predilection for disease development, and the majority of cases did not recover despite treatment. This data supported anecdotal experiences of practitioners in the field.

Chapter 3 put into practice an epidemiological principle when a new or unknown disease is encountered: a case-control study. Based on the causal diagram, limited published literature,

and anecdotal experiences the work in this chapter helped to identify potential risk factors for TTNS. Interestingly, bovine viral diarrhea virus, vasculitis and apical sole thinning were shown to have an association with TTNS. A case-control study does not have the ability to prove causation; however, the risk factors identified can lead to further, more specific studies to quantify their biological significance.

Project limitations included the inability to investigate the role of *Treponema* spp. in toe tip necrosis. There appears to be an increased prevalence of dairy steers being fed in Alberta feedlots, and as such, a potential role for transmission of this pathogen in the environment. Since earlier work in the UK has identified a role of *Treponema* spp. in *toe* necrosis, not toe tip necrosis, in dairy cattle it would have been important to pursue this aspect when risk factors were evaluated. Another major limitation in Chapter 2 was not having a denominator of animals in the database. The inability to determine risk of disease and specific lot level prevalence was a constraint on the results from the database.

Based on the work done there are multiple factors for the development of TTNS. It is clear that this condition develops in the arrival period to the feedlot. BVDV, vasculitis, and apical sole thinning have been implicated as risk factors for TTNS but their exact role in the pathogenesis is not as clear.

5.2 FUTURE RESEARCH

Future work that evaluates the time around transportation of animals from their origin to the feedlot would be essential. Specifically, looking for presence or absence of claw lesions prior to animal transportation and feedlot arrival. These animals would then be followed throughout the feeding period and monitored for disease development. Identification of farms, auction marts, and/or feedlots where continued clustering of TTNS occurs would be the first step to investigate the flooring design of facilities. Clinical trials that evaluates mechanical trauma as the inciting

cause such as placing a foot under a load of pressure on Plexiglas and assessing whether movement of the limb causes the white line to be stressed or disrupted. Behavioral trials that qualitatively measure the “hyper-excitability” of calves could be evaluated by hair cortisol concentrations or chute exit speeds. Lastly, micronutrient concentrations, especially zinc and copper, in the claw could be measured by mass spectrometry to assess claw integrity.

5.3 IMPLICATIONS

The research provided in this thesis has great implications for the feedlot industry. Most importantly, this work has provided a name for a condition that was often misdiagnosed due to a non-specific case definition. Also, these findings show that trained feedlot personnel can recognize early lesions that could allow for successful treatments and reduce the number of non-responding lame cattle. Lastly, this project has provided risk factors for TTNS that can be used in prevention and treatment strategies while further causal studies are investigated.

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APPENDIX A

The majority of cows will calve in the spring months (March to May). Most cow-calf producers aim to calve within a few weeks of each other to target uniform weights in the calf crop, and as such, will aid in marketing all calves as a group. Prior to pasture turn-out the male calves are generally castrated, but also can be performed within a few days of birth, and thus a bull calf is referred to as a steer, and a female calf is called a heifer. When these calves are approximately two-three months old, the cow-calf pair is turned out to pasture for the summer months (June-August) where the pair grazes grass and continues to grow.

During the fall months (September-November) these cows and calves are herded together and brought in from the summer pasture. During this time the calves and cows are separated from each other in a process called weaning. The cows will have been exposed to a bull during the summer months and should be pregnant for the cycle to start the following year. The calves' weight will vary between 600 lbs (272 kilograms) to 900 lbs (408 kilograms) and will be mature enough to grow and thrive on their own. Most cow-calf producers will sell the current year's calf crop to another producer that specializes in back-grounding or finishing the calves to a targeted slaughter weight. Heifers can be retained by the owner as replacement heifers to maintain and offset older breeding cows in the herd whereas steer calves are often sold for meat.

Generally, calves will leave the farm between six and 12 months of age. Calves that are weaned and sold through an auction mart system are termed auction-derived calves. Groups of uniform weight calves purchased directly from pasture into a feedlot are termed ranch-direct calves. Lighter weight or younger calves that continue to graze on grass or other forages during the winter months until 12 to 16 months of age or an anticipated target weight of 900 lbs (408 kilograms) are called back-grounded calves. Between nine and 11 months of age calves will

enter a penned feeding yard, known as a feedlot, where these animals will be fed increasing quantities of grain mixed with forage to a weight of 1350 to 1400 lbs prior to slaughter.

However, some calves are finished on grass prior to slaughter and are referred to as grass-fed.

The majority of calves, aged six months to 11 months of age, or yearlings, which are animals at or greater than 12 months of age, will be transported to the feedlot destination by low stock trailers or livestock semi-trailers. Ramps, pens, and alleyways are required to load groups of cattle onto these trailers. Cattle can be loaded on the trailer for long distances (> 400km) at a time (Gonzalez *et al.*, 2012). There are federal regulations that ensure animals are transported within certain timeframes, have adequate ventilation, and appropriate stocking densities.

Often groups of cattle are purchased from a seller, which come from a similar source or contain the same breed of cattle and are referred to as a "lot" which is a group of cattle. Once cattle arrive at the feedlot it is common practice in western Canadian feedlots to process cattle within the first 24 hours after arrival. This involves administration of vaccinations, topical parasiticides, identification, and animals are sorted into similar age and weighted groups. This mixing of cattle, regardless of original source of animals, allows the feedlot to have uniformity and consistency of animals prior to slaughter. The alleyway and holding facilities in which cattle are processed are often made with iron, wood, or pipe that are placed on concrete or iron-grated floors with gravel to aid in traction for the animal. From these processing areas cattle are moved into an outdoor, dry pen that contains a range of 200-400 head of cattle.

Cattle have ample room to move, eat at a bunk, and drink water in these pens. A starting ration for a 450-600 lb calves coming from pasture into the feedlot is largely comprised of forage or roughage, such as hay. Diet composition changes as the animal grows and develops to a grain or concentrate-based diet, such as corn or barley. A grain fed diet produces tender, and flavored

marbled beef. A finished feedlot animal diet will consist roughly of 90% grain at the end of the feeding period to achieve a weight of 1200-1400 lbs. On average, cattle will spend 60 days to 200 days in a feedlot before their optimum finished weight is met prior to slaughter.

APPENDIX B

FORM 1: Data collection form used by veterinary practitioners.

Data Collection Form

Date: _____ Submitting Practice: _____

Feedlot ID: _____

Animal ID and diagnosis (use a separate form for each case and control animal):

Case ID: _____ Case Diagnosis: _____

Control ID: _____ Control Diagnosis: _____

1. Formalized Sample (for each case and control animal):

- Left papillary Muscle (X 2) Interventricular septum

2. Feet and Swabs:

- Feet (include both hind feet if one hind is affected or both front feet if one front is affected)

Location of Lesion (circle foot and claw)

Front foot:	Left	Right
Claw:	Medial	Lateral
Hind foot:	Left	Right
Claw:	Medial	Lateral

3. Secondary affected tissues, if possible:

- Formalized (i.e.: tendons, lungs etc.) _____
- Swab (i.e.: tendons, lungs etc.) _____

Please accompany this form and the individual animal feedlot record with the samples. Pair the case/controls by packaging together or note the pairing on this form. Double-bag and refrigerate or freeze the feet. Avoid shipping on weekends.

IMAGE 1: Apical white line separation (Feedlot Health Management Services; 2012).



IMAGE 2: Sagittal section of apical white line separation and pedal osteitis (Feedlot Health Management Services; 2012).

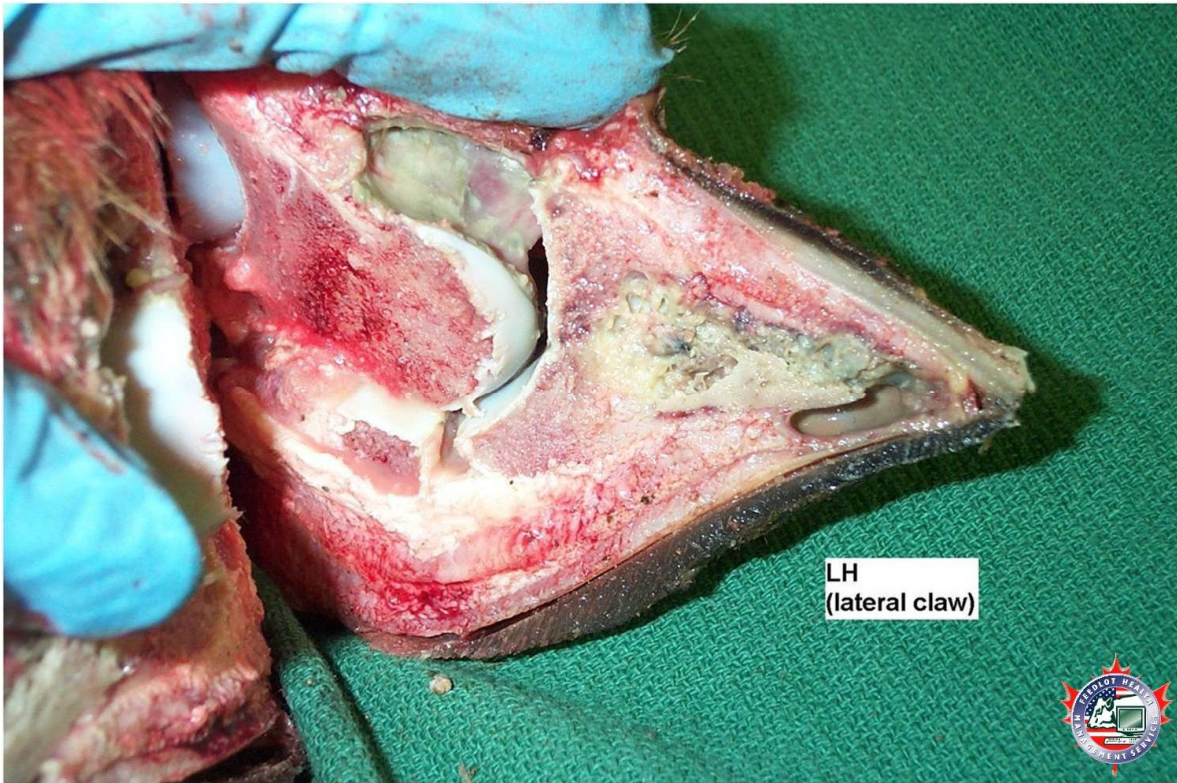


IMAGE 3: Evidence of embolic pneumonia in a feedlot animal (Feedlot Health Management Services; 2012).

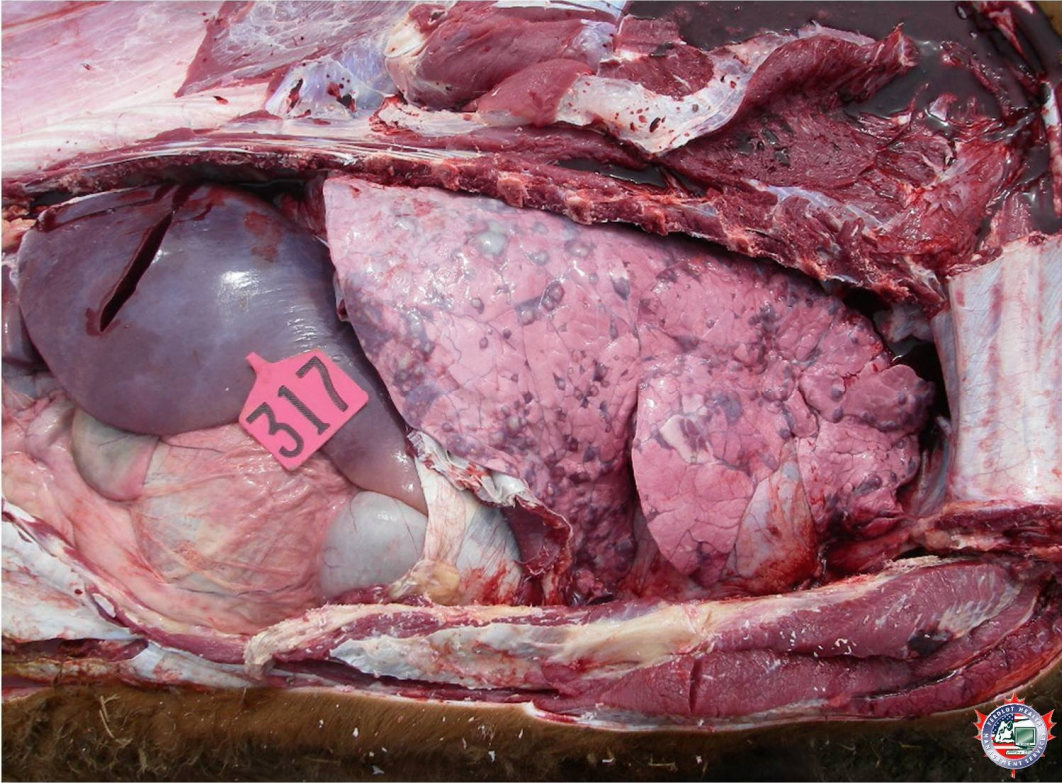


IMAGE 4: Evidence of hindlimb cellulitis secondary to toe tip lesion in a feedlot animal (Veterinary Agri-Health Services; 2012).

