Contagious Ecthyma Dermatitis as a Portal of Entry for Erysipelothrix rhusiopathiae in Muskoxen (Ovibos moschatus) of the Canadian Arctic

Contagious Ecthyma Dermatitis as a Portal of Entry for Erysipelothrix rhusiopathiae in Muskoxen (Ovibos moschatus) of the Canadian Arctic Matilde Tomaselli,1,2,7 Bjørnar Ytrehus,3 Tanja Opriessnig,4,5 Pa´draig Duignan,2,6 Chimone´ Dalton,2 Susan Kutz,2 and Sylvia Checkley2 1 Polar Knowledge Canada, Canadian High Arctic Research Station, 1 Uvajuq Road PO Box 2150, Cambridge Bay, Nunavut X0B 0C0, Canada; 2 Department of Ecosystem and Public Health, Faculty of Veterinary Medicine, University of Calgary, 3280 Hospital Drive NW, Calgary, Alberta T2N 4Z6, Canada; 3 Department of Biomedical Sciences and Veterinary Public Health, Swedish University of Agricultural Sciences, Box 7036, 750 07 Uppsala, Sweden; 4 The Roslin Institute and The Royal (Dick) School of Veterinary Studies, University of Edinburgh, Midlothian, UK; 5 Department of Veterinary Diagnostic and Production Animal Medicine, College of Veterinary Medicine, Iowa State University, Ames, Iowa, USA; 6 The Marine Mammal Center, 2000 Bunker Road, Sausalito, California 94965, USA; 7 Corresponding author (email: matilde.tomaselli@polar.gc.ca)

ABSTRACT: Erysipelothrix rhusiopathiae was de□tected immunohistochemically in contagious ec□thyma (orf virus) dermatitis in two muskoxen (Ovibos moschatus), harvested and found dead in 2014 and 2015, respectively, on Victoria Island, Canada. This may help target further research on E. rhusiopathiae epidemiology and mechanisms of infection in muskoxen, recently associated with widespread mortalities in Canada's Arctic

Erysipelothrix rhusiopathiae is a facultative, anaerobic, gram-positive bacillus found ubiq□uitously in nature in both the terrestrial and marine environments (Wang et al. 2010). To date, 28 serotypes within the Erysipelothrix genus have been recognized worldwide from a range of vertebrates (including humans), invertebrates, water, and soil (Wang et al. 2010). Depending on intrinsic virulence factors and host immunity, E. rhusiopathiae can be a pathogen or a commensal, as well as a saprophyte (Wang et al. 2010). Disease ranges from localized to generalized cutaneous le□sions to potentially fatal septicemia associated with endocarditis or polyarthritis (Wang et al. 2010). Immunization against E. rhusiopathiae is common in farmed animals—especially in the swine, poultry, and ovine production systems—to avoid losses caused by acute and chronic erysipelosis (Wang et al. 2010). In free-ranging wildlife, E. rhusiopathiae has been associated with widespread mortalities of muskoxen (Ovibos moschatus) between 2009 and 2013 on Banks and Victoria islands in Canada's Arctic (Kutz et al. 2015; Forde at al. 2016; Tomaselli et al. 2018). Preliminary whole-genome sequencing and phylogenomic analyses of E. rhusiopathiae isolates from the muskoxen found dead at those locations suggested limited heterogeneity compared with mainland isolates, supporting the hy□pothesis of a recent pathogen introduction on these islands (Forde et al. 2016). However, a recent retrospective serology study document□ed that E. rhusiopathiae has probably been circulating longer in muskox populations: seropositive animals were found among the earliest tested sera from different locations (1976 in Alaska, US; 1991 on Banks Island, Northwest Territories, Canada; and 2011 on Victoria Island, Nunavut, Canada); seroprev□alence was also greater in association with unusually high mortality rates and population declines (Mavrot et al. 2020). It remains unclear whether a more-infective and virulent E. rhusiopathiae genotype has emerged on Banks and Victoria islands in recent years or whether ecologic conditions have changed, triggering a web of disease causation, includ□ing novel pathogen interactions. In the same geographic area of Canada's Arctic, contagious ecthyma (orf virus) has also been recently described in muskoxen (Toma□selli et al. 2016; Dalton 2019; Rothenburger at al. 2021) as an emerging or re-emerging pathogen (Tomaselli et al. 2018). Contagious ecthyma is caused by the orf virus, a DNA virus belonging to the Parapoxvirus genus of the Poxviridae family, which can infect both animals (domestic and wild ungulates) and humans. The virions are extremely resistant in the environment, where they can remain

infective for several years in shed scabs (Hargis and Ginn 2012). Proliferative lesions are generally found on the skin of the head, the lower legs, and on mucocutaneous junc□tions and appear as a superficial, thick, brown or gray crust, commonly ulcerated (Vikøren et al. 2008). Ulcerated lesions can be extremely painful, limiting the ability of infected animals to feed or walk properly (Vikøren et al. 2008), and affected mothers often abandon their suckling calves, possibly due to painful udder lesions (T. Bretten, personal communication). Although orf lesions are typically more severe in juveniles (calves and yearlings), natural infection does not confer long-term immunity; animals at any age can be reinfected and develop proliferative dermatitis (Hargis and Ginn 2012). Severe infection can lead to mortality by starvation or predation and may predispose an animal to secondary fatal infections by providing an entry point for opportunistic bacteria, which was recently described in one orf-infected muskox calf from the same study population that died from Corynebacterium freneyi septicemia (Rothenburger at al. 2021). In human medi□cine, orf viral dermatitis has been described, predisposing the patient to cutaneous inocu□lation of E. rhusiopathiae, resulting in a severe form of disseminated erysipeloid in an English sheep farmer (Connor and Green 1995) We present findings from two muskoxen, one adult bull hunter-harvested on Victoria Island (708010 4800N, 1078340 1000W) in August 2014, and one adult cow found dead in the same region (698060 2900N, 1058180 600W) in June 2015. The bull had proliferative derma□titis of the right hind limb (Tomaselli et al. 2016), whereas the cow had perioral lesions (Fig. 1A, a, B, b). In both cases, orf virus infection was confirmed by histopathology and conventional PCR targeting the major enve□lope protein gene (B2L) performed at the Veterinary Diagnostic Laboratories of the University of Calgary following methods described in Tomaselli et al. (2016). Forma□lin-fixed, paraffin-embedded skin lesions were then processed by immunohistochemistry (IHC) using E. rhusiopathiae polyclonal antiserum at the Veterinary Diagnostic Lab oratory of Iowa State University, as described by Opriessnig et al. (2010), and tested positive for E. rhusiopathiae (Fig. 1C, D). For completeness, we report that orf skin lesions of four other muskoxen found dead in 2015 in the same geographical area were negative for E. rhusiopathiae by IHC. How□ever, the IHC technique currently available specifically targets the E. rhusiopathiae sero□types 1a, 1b, and 2—those that are most frequently associated with clinical disease in pigs. Although limited information is currently available on the serotypes of the E. rhusiopa□thiae isolates associated with the muskox die□offs on Banks and Victoria islands, one belonged to serotype 1b (Forde et al. 2020) and another to serotype 5 (Forde at al. 2016). Genomic analyses revealed that the latter was likely the most-prevalent serotype among the die-off isolates (Forde at al. 2016), but it is not targeted by the IHC test. Given the limita□tions of the current IHC technique available, we cannot exclude the possibility of false□negative results for at least some of the other animals. To understand drivers of recent muskox mortalities, we suggest further exploration of whether the orf virus may have a significant role in predisposing animals to fatal infections from E. rhusiopathiae, given that it produces wounds that can facilitate secondary bacterial infection with subsequent septicemia. This could be important considering that orf virus appears to be increasingly found in muskoxen at different locations across their range (Afema et al. 2017; Tomaselli et al. 2018; Dalton 2019), including in areas of both Canada (Banks and Victoria Islands) and Alaska (eastern North Slope), in which declines and mortalities have been observed and were temporally associated with high E. rhusiopathiae seroconversion rates (Mavrot et al. 2020). We thank Cambridge Bay harvester Jorgan Aitaok Sr., the Cambridge Bay conservation officers Shane Sather and Candice Pedersen, High Arctic Lodge Outfitting, DALL Aviation, and the pilot William Brady who helped to locate and access the animals. Special thanks to Donald McLennan and Johann Wagner for field support, the Kutz research laboratory and the Veterinary Diagnostics Services of the University of Calgary and the Iowa State University, especially James Wang, Susan Calder-Lodge, and Betty Pollock for excellent laboratory support, and Taya Forde. This study was funded by the University of Calgary, ArcticNet, Canadian Wildlife Health

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